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The Journal of Neurology and Psychopathology

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THE JOURNAL OF NEUROLOGY AND PSYCHOPATHOLOGY

Vol. XII. OCTOBER, 1931. No. 46.

Original Papers.

THE BIOLOGICAL SIGNIFICANCE OF EXTRA-PYRAMIDAL SYNDROMES, APROPOS A CASE OF WILSON'S DISEASE IN THE ADULT:

Second contribution to the biology of extrapyramidal affections.

By

R. MOURGUE, Mulhouse, France.

'In all the functions of the living organism, without exception, there is an ideal and a material side. By its form the ideal side of function is linked to the unity of the plan of creation or construction of the organism, whereas the material side corresponds by its mechanism to the properties of living matter.'—Claude Bernard (Discours de réception à l'académie française, 1869).

During the last fifteen years the number of studies devoted to extrapyramidal syndromes has been so considerable as to require a large volume for their exposition. Detailed researches, of very unequal value in point of fact, abound; but so far as I know the question of the biological significance of the subject—in the sense, as we shall see, of the totality of phenomena, regarded as most characteristic, embraced under the not very happy term 'extra-pyramidal'—has not as yet been approached. In a preceding essay, published some years ago, I showed, apropos a case of torsion spasm, that this class of morbid phenomena, far from being purely and simply synonymous with an affection of the central ganglia, according to the classical doctrine, involved in reality the organism as a whole. It is this aspect which I shall try to render precise from a biological viewpoint, taking as text and example a case of hepato-lenticular syndrome or Wilson's disease in the adult which has been followed closely during nearly the whole of its evolution. This latter condition is of capital importance for the biological standpoint, which ascribes prime significance to evolution in time.

CLINICAL OBSERVATION.

1.—M. Ab., shoemaker, age 46. *Family history:* Nothing of importance. *Previous history:* For seven or eight years it had been remarked that at intervals 'his eyes were yellow.' Four days after an emotional experience conjunctival icterus occurred,

The actual affection dates back some two and a half years. The earliest symptoms were pains in the stomach and left hypochondrium, without vomiting or loss of appetite. Thereafter, a continual diurnal cough developed, with pharyngeal irritation. Some paresis of the pharyngeal musculature followed, revealed by inability to spit and trouble in deglutition. Only liquid nourishment has since been taken. During the last two months dysarthria has become pronounced. For two or three months tremors have been in evidence and become worse. They cease in the recumbent position. From the onset, muscular rigidity has been complained of, and been progressive (it appeared as though the arms and the muscles of the neck were being 'pressed in a vice'). His wife noticed reduction of the stiffness during sleep, and greater distinctness of articulation in the mornings. Difficulty in defæcation was remarked.

From a psychical standpoint, his wife affirmed strongly that ever since his marriage (fifteen years previously) she had observed intermittent conjunctival icterus, apart from any clinically recognisable hepatic affection, chiefly with any slight contrariety. Increasing irritability alternated with phases of depression, and unmotivated attacks of spasmodic weeping occurred. Memory and orientation were normal.

On examination: Rigid facies; the head is always held in the same position. Fixed expression, with eyelids seldom lowered. Parkinsonian attitude, but with head and trunk in hyperextension. Considerable dysarthria; speaks as though his mouth were full, according to his own expression. With fingers extended, there is mild tremor of their extremities; no intention-tremor of the classical kind (can drink a glass of water without any shaking), and none when at his occupation. Tremors appear during certain complex actions (dressing, arranging his necktie) belonging to the group of cupraxias. The movement is performed slowly and is decomposed into a number of phases with a slight pause between each. Cutaneous and tendon reflexes normal, except for exaggeration of the knee-jerks without clonus. They cannot be inhibited by 'volition.' Postural segmental reflexes (Westphal-Foix): exaggerated. Oculo-cardiac reflex: 73 before compression, 82 after. Internal and external ocular musculature: normal. Fundi: normal. Wassermann reaction: negative in blood and spinal fluid (Institut Pasteur and Dr. Peyre). Spinal fluid: normal. Urine and blood: see below.

2.—Aug. 14, 1920.—Says he has felt inclined to weep the whole morning, for no reason, explaining that it starts if he contracts the upper facial muscles; 'I wish to control myself, but I can't; it rather annoys me.' Asked whether there is the same sadness as when he experiences a genuine chagrin, his answer is: 'when I weep for a real sorrow, I sob; when I weep as I am now doing, it is not the same thing. I feel the former comes from my heart; but now I am weeping in spite of myself; I feel it comes from the stomach. If I am commiserated with, I am compelled to cry; if I experience enjoyment, I have also the inclination to weep. When I weep, I feel as though I were being gripped (indicating the epigastric region); it is difficult to explain what I actually feel. It seems as if my stomach were shrivelling, and that ends up with pains.' He has often had nightmares (dreams he is fighting, falling, or crying 'thief!').

3. Oct. 3, 1920.—The patient made the following comments spontaneously. 'I have the inclination to cry for no reason, it is because of my great feebleness. When I feel stronger, I am more merry. When I start to walk, sometimes my legs give way under me, but after walking a minute my powers come back. The further I go the greater the tendency to fall forward; formerly it used to be backward. Often enough my head is confused; it seems like a mist, which may last ten minutes. On getting up in the morning, if I do not pay attention I should fall; my balance fails me. Sometimes there is a tendency to go right or left, sometimes forward. My mouth is always full of a thick and sticky saliva. Sometimes there is frequency of desire to micturate without my passing much, in the mornings; sometimes I pass water till it stops; I feel I could pass more but the power fails me.' Sometimes urination is precipitate.

4. Nov. 12, 1920.—During my absence a medical man not acquainted with the nature of the affection administered ·15 cgm. neosalvarsan Billon by injection into the gluteal region (Oct. 21). Three days later, cutaneous and conjunctival icterus appeared; from that date, it became intermittent. Further, since the injection tremors have developed; when lying down the patient exhibits marked tremor of the toes, with involuntary twitches in arms and calves. Difficulty in defæcation; intense salivation (like an encephalitic), of parasympathetic type; pollakiuria; dysarthria and dysphagia (swallows even fluids with trouble). Great feeling of fatigue, *even without muscular effort*. Sensation of pressure in muscles of neck. All these symptoms are more pronounced on the left side.

5. Nov. 24, 1920.—Feeling of great coldness especially in the extremities, unrelated to external temperature. Spasmodic weeping more frequent, always accompanied by epigastric pain. Micturition and defæcation always troublesome. For some days has

Fig. 1. Photograph of patient taken several years before apparent commencement of first symptoms.

noticed between eleven o'clock and noon 'stiffening,' more marked on the left side. Salivation unaltered; loss of weight though alimentation is normal.

6. Dec. 27, 1920.—Some fifteen days ago he believed himself cured, for a day or so; assured me that all his symptoms had vanished. Now complains that external cold aggravates his muscular rigidity. Subjectively, the left side is colder than the right. From the point of view of his trade, he cannot smooth off, but can use the hammer well; cuts the leather with the knife without shaking. He declares that rigidity has diminished while trembling has increased during complex actions. Deglutition easier, and dysphonia rather better. No subicteric tinting of the skin. Gross trembling of the tongue; boulimia ('I eat four times a day'). Walking presents distinct difficulty in starting, being shaky to begin with; it then becomes more and more assured. Exhibits antero- and lateropulsion; formerly felt himself 'pushed' backward.

7. Dec. 28, 1920.—Complains bitterly of difficulties in micturating. Passes water twenty times in a few hours. Is not relieved by the act. Sometimes has the desire without

the power. Has insight into his condition in the sense that he fears becoming unable to work at some time. Normal orientation. States that when he is 'weak' vision also becomes 'weak,' meaning thereby having the 'sensation of fatigue,' of pressure in the neck, stomach shrinking, pains like rheumatism over the left shoulder-blade, but also elsewhere, for the pains are not always in the same place. The superficial venous network of arms and legs, especially distally, is very noticeable; the muscles stand out sharply. In the erect position, fibrillary trembling of leg muscles. Shaking of hands during undressing. No defect of sensibility or of segmental attitudes; knee-jerks active, particularly the left; cremasteric, plantar, and achilles reflexes normal. Slight clonus of toes after forced flexion of foot on leg. No myotonic reaction in trapexius with pinching or faradic current.

8. Jan. 26, 1921.—Still complains of desire for micturition without accomplishment except under great difficulty. Similar trouble in regard to defæcation. As before, sleep is interrupted by nightmares (dreams he is 'falling over a precipice, thieves have entered his room, fighting'). In walking, anteropulsion and shaking of the legs. Muscular rigidity 'has now reached my thigh.' Sometimes feels the left side worse. Complains of vision being 'weak.' Speech is more and more defective, salivation more and more intense. Much depressed in view of his consciousness of the serious nature of his malady.

9. March 11, 1921.—Has given up all work at his trade. Walks *en bloc* without using the arms. Extreme slowness of movement. Considerable emaciation. Tremors of finger ends and of tongue accentuated. More frequent spasmodic weeping. Anteropulsion; sudden stiffening of muscles of neck and shoulders when walking. Deglutition and articulation always very defective, as well as defæcation. Feels much better when lying down. Reflex of Léri: absent.

10. March 18, 1921.—When he walks the left arm is held closer to the body than the right. Frequent deep sighing. Hypotonia of calf and arm muscles (where veins no longer in evidence), whereas thigh muscles remain rigid. From time to time, generalised fibrillary twitches confined to the hypotonic muscles. Violent itching at the level of the upper thorax noted for the first time. Brown pigmentation of the abdomen as high as the xyphisternum. Sensation of coldness in the calves. Deglutition more defective than ever.

11. March 25, 1921.—For a month has felt the right side of the body becoming weak. To-day, development of lower facial weakness on the right side, seen by drooping of the labial commissure on that side. Fixed expression, but no involvement of the oculomotor. Great feebleness of the muscles of the legs. The severe feeling of fatigue of which the patient is conscious seems to have coincided with the general diminution of tonus; when the calves were rigid he felt less tired. Shaking of the legs; lateropulsion to the right. Defæcation very difficult, with tenesmus. Normal orientation. Progressive general cachexia. Mimic expression of smiling preserved but dissociated, involving rather the upper part of the face (on the non-paretic side).

12. April 7, 1921.—Recently injections of scopolamine have been tried but abandoned because of their producing a clouded state of consciousness with a general sensation of coldness, especially on the face. During examination of the left plantar reflex, clonus of the contralateral great toe developed, spreading thence to the left. Continued for several seconds, then remained on the right side only. Remarked that these phenomena sometimes develop spontaneously, in 'little attacks.' They reappeared during further examination. When being tested for adiadocokinesia, he said that corresponded to what occurred in his feet, viz. appearance of clonic movements in the toes. On the left, the finger-nose test produced quick movement of the hand to about a few centimetres from the nose, when a sudden twitch followed. Remarks that when in the recumbent position he experiences a sensation of painful pressure in the epigastrium which disappears

whenever he sits up. When he lies down the exaggerated salivation does not occur. Micturition and defæcation as before. Constant diurnal drowsiness; sleeps heavily at night. For several months, hair falling out, though neither from scalp nor moustache.

Reflex of solar plexus (Claude): negative in spite of strong pressure. Oculo-cardiac reflex: 77 before and 73 after ocular compression.

13. April 14, 1921.—Adiadocokinesia persists, but the movement of arrest in the finger-nose test, noted above, is no longer found. Cannot stand on one leg even with eyes open. Knee-jerks: normal on the right, very brisk on left. During testing of plantar reflexes, same phenomenon of crossed toe clonus as before. In the erect position, hypertonus of leg muscles pronounced; in the recumbent position, extreme hypotonus of the same muscles, to such a degree that the fingers can be insinuated on the inner aspect of the tibia, between the posterior surface of the bone and the adjacent muscular masses. Paresis of the lower face as before. When the patient takes to his bed he cannot, with head lowered, support himself on his hand flattened out on the bed, but can do so with fist closed.

14. April 18, 1921.—When standing up to pass water he is obliged to use force; on palpation the muscles of the abdominal wall are strongly contracted. It is as though the vesical sphincter offered great resistance. After the passage of perhaps a cupful of urine, slight trembling of the whole body. After several minutes he is obliged to rise and micturate again, in the same way, to the amount of half a cup.

15. April 19, 1921.—To-day, about half past four, the patient spoke very distinctly without obvious dysarthria. After a series of trials, two hours later his voice became unintelligible. On the legs, where the hairs have fallen out, small black pigmented spots have appeared, like those produced by silver nitrate, as has already been noticed in respect of the abdomen.

16. May 28, 1921.—Pronounced pains, seemingly spontaneous, in both heels, which are not, however, painful on pressure. Says 'when I speak I have the same sensation here (epigastric region) as during the attacks of weeping.' Has two attacks of this in front of me, the first when I ask him how he is, the other when I hand him his photograph. Profuse sweating chiefly on the upper face, especially on the sides of the nose. Abundant perspiration with effort. Saliva thick and in quantity. At certain moments lachrymal secretion without apparent reason. Frequent tenesmus. When at stool he feels 'something which closes up.' Asthenia always extreme; can cut leather, but with great difficulty. Under the influence of emotion (mere entrance of a client into his shop) shaking of the whole body and enormous increase in dysarthria. In finger-nose test, slight arrest before the end of the movement. Cutaneous plantar excitation on the left side produces clonic movement of same and of opposite foot; stronger stimulation causes slight retraction of the opposite foot only. Right knee-jerk, considerable excursion of the leg; left, less, but sudden arrest and more voluminous swelling of quadriceps. When he performs any 'voluntary' act he 'stiffens to the mouth.' When he dresses, intense trembling of the whole body. Moans as he does so. Urination accompanied by very strong abdominal contraction as before.

17. June 17, 1921.—To the great surprise of his wife, dysphagia for solid food has disappeared completely during a fortnight; on the other hand, his speech is understood with difficulty even by her. Profuse sweating over the upper part of the face. Other symptoms unchanged.

18. June 22, 1921.—In the morning, persistent pain in the metatarsophalangeal articulation of the great toe and in the heel. Normal motility of external ocular muscles. Rectal temperature, taken night and morning for eight days, shows no alteration in thermal function.

19. July 7, 1921.—The patient states he feels a coldness in the left knee, less marked in the right. The result of the finger-nose test corresponds to the instinctive state of the

FIG. 2. Photograph of patient taken about three and a half years after apparent commencement of first symptoms.

moment; on the left (where the motor disorders have always been more noticeable), dipping and slight deviation before the nose is reached. Same observation on the right, but less in degree. With encouragement and assurance, the slowness of movement on the left diminishes, and the dip is scarcely noticed; on the right, the movement becomes almost normal and the deviation disappears. When any one enters he cannot reproduce this and says spontaneously that 'everything upsets me.' When in the erect position, on the request to relax completely, it is seen that the left forearm is more flexed on the upper arm and that the fingers are more flexed on the palmar aspect; the attitude recalls that of early hemiplegia (see fig. 2). When the foot is flexed on the leg, the tibialis anticus contracts and the posture persists for several minutes in spite of the request to 'let the foot go' (Westphal's paradoxical contraction).

It is impossible to get the patient to breathe quickly, but with slight acceleration there is marked tremor of the toes of the right foot, followed by spontaneous extension and fanning. After twenty minutes a second attempt at rapid respiration was made. A few seconds later, extension of the last four toes on the right, of the great toe on the left, and trembling of the former. The opened mouth has a definite oval shape with disappearance of the right naso-labial fold. Can appreciate correctly differences between weights on right and left; holds a weight of one kilo in the left hand, the arm semiflexed, for 55 seconds without being aware of fatigue, as is practically normal. Pressing the epigastric region causes what he calls 'weak attacks'; he attaches great significance to this part. Complete loss of libido sexualis since the commencement of the illness.

20. Aug. 5, 1921.—Sensations of formication and of coldness on the outer side of the left leg; on the outer side of the foot, a feeling of warmth. When he pinches the leg on its outer aspect the sensation of cold becomes one of heat. Says 'when I speak it is always in the stomach I become fatigued.' In order to be understood he has to speak slowly. His wife says he cannot pronounce a long phrase without having to stop. The tiredness felt in the legs varies in degree; it involves upper and lower limbs and spares the trunk. Defæcation, formerly difficult, has become rather easier. Micturition always difficult. Dysphagia continues. Recently, has had trouble in opening the mouth owing to forced contraction of masseters. Intermittent salivary hypersecretion.

21. Aug. 10, 1921.—During the night of Aug. 6, continual cough which ceased suddenly in the morning. Respiratory difficulty without any cause being found by auscultation. Feels better when the head is held forward. Says he would sleep sitting up if he could. Stools are of normal consistence; there is thus no constipation.

22. Aug. 25, 1921.—The more he speaks the greater is the fatigue, localised in the epigastric region. Spontaneous pains much less intense on the right side. Frequent spasmodic weeping with epigastric pain. Brownish pigmentation round the hair follicles in the midline of the abdomen persists. Constant stiffness of the neck. Walks without lifting heels. Conjunctival subicterus. Can no longer wear braces because of their traction on neck muscles. Cannot bear trousers closed over the epigastric region or wear collars at all tight.

23. Sept. 20, 1921.—Is at his worst between eleven o'clock and twelve noon. His wife is impressed with the great variability of his condition; from day to day and even from hour to hour modifications occur in his physiognomy; his neck alters in volume similarly, the same shirt-collar sometimes annoys him, sometimes not (variations in size of thyroid observed). At night, pains in heels and buttocks; last two days, in the left arm. Speech now incomprehensible. Scopolamine and liver extracts are the sole medicaments producing a little satisfaction.

24. Sept. 28, 1921.—When walking, throws the left leg forward more than right and uses the right arm in balancing, not the left, which adopts a hemiplegic position. Considerable dysphagia. Continual trembling of toes; trophic disorder of the left great toe. No definite pyramidal signs. No evidence of catatonia.

25. Nov. 22, 1921.—Paroxysmal pains in the left arm. Vesical and rectal symptoms more pronounced. No appetite; much emaciation. It is remarkable that the dysphagia disappears when his attention is concentrated on the act of swallowing. Increasing muscular asthenia. Gross fibrillary tremors of tongue. Marked intention-tremors. Weeping more frequent; sometimes suffocating attacks. Speech low in tone, but perceptible and normal at the commencement of talking, dysarthria following after a few minutes.

26. April 15, 1922.—Still no pyramidal signs; for efforts of brief duration no loss of muscular force. Dysuria worse than ever; trembling attacks of a generalised kind when trying to micturate at night. Two important points are now in evidence; (1) the erect attitude is no longer one of hyperextension, the head being lowered and the back slightly curved; (2) the right side is as much affected as the left. Cannot dress himself. Disorder of deglutition has disappeared; dysarthria as before, but when insistence is made on the matter he can make his unintelligible speech become quite clear. Desquamation of the whole of the skin except on the face. Generalised tremors with any contrariety. Advanced trembling *en masse* of the tongue. Hands very cold, sometimes violet in colour; respiration shallow, intermittent conjunctival subicterus. Loss of cremasteric reflex. Kohnstamm's phenomenon of catatonus evident in the upper limbs. Extreme fatigability; diminished amplitude of movements; wide movements are accompanied by tremors and moans. Continual salivation. 'Voluntary' opening of mouth limited, but complete on yawning. Cutaneous pigmentation of abdomen reduced.

27. June 16, 1922.—Intermittent swelling of feet and ankles (no albuminuria). Occasional congestion of head (cheeks and ears particularly), which makes his head 'feel bigger.' Brownish pigmentation on buttocks. Desquamation of skin. Deglutition takes place normally.

28. May 27, 1923.—During the last year has been tormented continually by dysuria. Two urologists separately have demonstrated that bladder and prostate are normal.

29. June 27, 1923.—Intense salivation and muscular asthenia; Parkinsonian posture of trunk. Under the influence of powerful emotion (death of a parent) complete urinary and fæcal incontinence.

30. Nov. 3, 1923.—His wife writes that 'at present his condition is not too bad; he has an appetite and swallows without trouble, while his articulation is more distinct. I note that when his condition seems better he tends to make bizarre and irrational statements; this is fleeting, and curiously enough, when it is pointed out to him he becomes aware of it and can remember what he has said. Disturbed nights, the patient jumping up in dreams and speaking at the top of his voice; if I answer him, he converses for a moment even though asleep. Difficulty of defæcation—in the case of his bladder, variable.'

31. Nov. 15, 1924.—His wife writes: 'My husband spends his days as if ankylosed, dosing in a chair, his eyes shut; if he walks, his head and chest are carried forward. Trouble at stool severe; urination is never regular. Speech unintelligible, more at one time than another; always salivating; great difficulty in swallowing liquids. Dreams much and talks in his sleep. Has two small sores on his hips which I have managed to dry up with ether.'

32. Sept. 8, 1926.—After progressive cachexia the patient died suddenly on August 20, 1926. In spite of every request the family refused an autopsy. During the last months his condition was as follows: sacral bedsores, asthenia, violent pains in arms, variability of symptoms referable to bladder, rectum, speech. In the case of the last of these, however, spoke to himself, towards the end, with complete unintelligibility. Nail of great toe enormously hypertrophied. Stiffness of neck largely disappeared. Parkinsonian attitude of trunk and head. For some months, no spasmodic weeping; persistent salivation; no particular defect of memory.

The illness extended over eight years; no hereditary factor was found on enquiry among other members of the family. No history of influenza or other febrile attack suggestive of the possibility of epidemic encephalitis was discovered to account for the disease.

Urinary analyses (M. Charles Guillaumin).

1. Dec. 3, 1920.—Lacto-vegetarian dietary.

Amount examined: 950 c.c. Density at 15° C.: 1022.

	Total for 24 hours.	Normal variations.
Total nitrogen (as N)	7·89	14—16
,, ,, (as urea)	16·95	30—34
Urea	13·92	24—28
Sal ammoniac (and amino-acids titrable in formol) (as NH_3)	0·42	0·70—0·90
Creatinin	1·00	1·30—1·60
NaCl	13·48	12—15
Urobilin		traces
Urological percentages:		
Nitrogen of urea	82·0	82—83
Ammoniacal nitrogen	4·4	5—5·5
Creatinic nitrogen	4·7	3·4—3·8
'Urogenic defect' (Maillard)	5·1	6—6·5

2. Dec. 21, 1920.—Lacto-vegetarian dietary.

Amount examined: 2,000 c.c. Density at 15° C.: 1,021.

Total nitrogen (as N)	12·80	14—16
,, ,, (as urea)	27·40	30—34
Urea	24·20	24—28
Sal ammoniac, etc. (as NH_3)	0·44	0·70—0·90
Uric acid	0·70	0·60—0·80
Purin bases (as xanthin)	0·08	0·05—0·12
Creatinin	1·70	1·30—1·60
Creatin (as creatinin)	nil	0—10% of the creatinin
Nitrogen (unallotted)	0·26	0·60—1·10
Total minerals	40·70	16—22
NaCl	25·40	12—15
Minerals (achloric)	15·30	4·75—6·75
Acidity (as P_2O_5)	0·82	1—1·20
Phosphoric acid (as P_2O_5)	2·30	2—2·40
Biliary acids	0	0
Biliary pigments	0	0
Urobilin	slight	traces
Urological percentages:		
Nitrogen of urea	88·3	82—83
Ammoniacal nitrogen	2·9	5—5·5
Purin nitrogen	1·8	1·8—1·9
Creatinic nitrogen	4·9	3·4—3·8
Nitrogen (unallotted)	2·1	7—8
Urogenic defect (Maillard)	3·7	6—6·5
Metabolism of nucleins:		
$\frac{\text{Purin bases}}{\text{Uric acid}}$	11	7—17
$\frac{\text{Phosphoric acid}}{\text{Total nitrogen}}$	17·8	14—15

Comment of M. Guillaumin: 'In view of the diet I expected to find very different figures. I repeated certain examinations, notably total nitrogen, with the same result. The remarkable lowering of the ammoniac and similarly the increase of the nitrogen percentage may be attributed to the high content of alkaline minerals.'

3. Jan. 28, 1921.—Creatinin (colorimetric method of Jaffé-Folin): 1 gr., 24 per litre.

4. April 12, 1921.—Ditto, 1 gr., 01.

5. May 1, 1921.—Indoxyl (indican)	..	abundant	traces
Scatolic red	.. ..	abundant	traces
Indol	.. .. ..	abundant	traces
6. July 18, 1921.—Urea	.. .. ..	18·15 per litre	19—22
Ammoniac	.. ..	0·82 ,, ,,	0·70—0·85
Total nitrogen	.. ..	14 ,, ,,	11—12
7. Aug. 12, 1921.—Urea	.. .. ..	9·71	19—22
Ammoniac	.. ..	0·18	0·70—0·85
Total nitrogen	.. ..	5·60	11—12
8. Sept. 2, 1921.—Urea	.. .. ..	10·50 per litre	19—22
Ammoniac	.. ..	0·34 ,, ,,	0·70—0·85
Total nitrogen	.. ..	5·35 ,, ,,	11—12
N of urea	.. ..	4·89 ,, ,,	8·8—10·5
NaCl	.. .. ..	10·52 ,, ,,	8—10
Creatinin	.. .. ..	present	
Ureic N to total N	..	91·4%	84—91%
NaCl to urea	.. ..	100%	42%
9. Sept. 23, 1921.—Urea	.. .. ..	16·50 per litre	19—22
Ammoniac	.. ..	0·84 ,, ,,	0·70—0·85
Total nitrogen	.. ..	8·85 ,, ,,	11—12
N of urea	.. ..	7·68	8·8—10·5
NaCl	.. .. ..	13·45 ,, ,,	8—10
Creatinin	.. .. ..	nil	
Ureic N to total N	..	86·7%	84—91%
NaCl to urea	.. ..	81·5%	42%

10. Feb. 7, 1921.—Examination of fæces (M. A. Lesure):

Hydrobilirubin	.. .. very small amount
Hydrobilirubinogen	.. traces
Biliverdin	.. .. none
Bilirubin	.. .. none

Conclusion: fæces only contain a quantity below the average of transformed biliary pigments and none of normal pigments.

Cytological examination of the blood.—The following examinations were made in the laboratory of Prof. Sabrazès at Bordeaux.

1. Jan. 7, 1921.—No poikilocytes, basophil granules or polychromatophilia. Most of the globulins have agglutinated. The number of whites does not appear notably augmented, it is certainly not decreased.

Leucocytic formula:

Polynuclear neutrophils	.. .. 57·1%
Mast-leucocytes	.. .. 0·4%
Lymphocytes	.. .. 37·1%
Large mononuclears	.. .. 3·6%
Large mononuclears (lobed nuclei)	.. .. .. 0·4%
Lymphoblasts	.. .. 0·4%

Nuclear value of 100 polynuclear leucocytes: 341.

Sometimes one up to four minute nuclear fragments are seen in a polynuclear leucocyte. Summary: absence of eosinophilia; relative lymphocytosis; nuclear value of polynuclears above average (deviation of nuclear picture to the right).

2. Jan. 19, 1921.—Examination by Prof. Sabrazès himself. No anisocytosis or poikilocytosis. Proportion of granular reds practically normal (not more than 1 or 2 per 1,000). Blood-plates rather above the average.

Leucocytic formula:

Lymphocytes	18%
Monocytes	4%
Monocytes with plurilobar nucleus	1%
Neutrophil polynuclears	76%
Eosinophils	0·6%
Mast-cells	0·6%

Nuclear value of 100 neutrophils: 316 (above normal).

Summary: fairly well marked neutrophil polynucleosis; reduction of eosinophils. Neutrophilia fits in with sympathicotonus; in vagotonus there is generally eosinophilia.

3. April 21, 1921.—*Digestive hæmoclasis test.*

Ingestion of 200 gr. of milk fasting, with examination of blood each twenty minutes after.

	Before test.	20 mins. after ingestion.	20 mins. later.
Polynuclear neutrophils	44·2	58·02	68·84
Lymphocytes	38·4	33·7	23·4
Mononuclears	12·6	3·7	4·26
Mononuclears (lobed nucleus)	3	0·96	2·25
Eosinophils	0·9	1·73	1·5

Summary: Before test, marked lymphocytosis and corresponding diminution in percentage of polynuclear neutrophils; after, increase of latter and diminution of lymphocytes and monocytes.

Pharmacodynamic tests.—Adrenalin. Subcutaneous injection of 1½ mgr. adrenalin (Clin) provokes after twenty minutes extremely marked tremors of hands during purposive movements, also of tongue and respiratory muscles (as pneumograms show); speech does not undergo any change. After twenty minutes, sudden cessation of tremors; they then begin again. During the test the patient looks exactly like a true case of paralysis agitans.

Atropin (March 18, 1921).—10.50 a.m. Pulse 80 per min. Subcutaneous injection of 8 mgr. atropin on outer aspect of left forearm.

11.10 a.m.=68 pulsations. Disappearance of all fibrillary twitches.
11.20 a.m.=72
11.30 a.m.=68
11.43 a.m.=72
11.45 a.m. Development of horizontal nystagmus of fine amplitude.
12 noon=76. Intermittent nystagmus. Slight mydriasis.

Pilocarpine.—Owing to a tendency to loss of consciousness with sensation of impending death produced by injection of 1/10 mgr., the test could not be carried out properly.

Scopolamine.—4.55 p.m. Pulse 76. Subcutaneous injection of ¼ mgr. scopolamine bromhydrate.

5.20 p.m. Intermittent horizontal nystagmus.
5.21 p.m.=76 pulsations.
5.40 p.m. Persistence of nystagmoid jerking.
5.42 p.m.=76 pulsations.
5.50 p.m. Persistence of nystagmoid jerking.

If now we attempt to characterise the preceding clinical picture, there will be, we believe, unanimity as regards its belonging to the group of hepato-lenticular syndromes; in more precise fashion we shall willingly affirm that it is a case of Wilson's disease in the adult. Without taking part in the scholastic discussions of nosologists, we shall refrain from speaking of pseudo-sclerosis, in the first place because Westphal himself, in his paper of 1883, said that was not a very happy expression (' nicht sehr glücklich '), and in the second, because all kinds of heterogeneous facts enter not only into his own confused cases, but also into those, even more confused, of Strümpell (1898).

ICTERUS.

It is convenient, at the outset, to draw attention to the following peculiarly interesting feature. Thirteen years before his illness seemingly began the patient exhibited intermittent conjunctival icterus and was subject to emotional icterus. This fact is extremely interesting in view of the discussions still going on relative to the connexion between the hepatic and the striate and other cerebral lesions. It is well known that Wilson has declared for the primary character, in all probability, of the hepatic dysfunction. Yet all researches on the production in the animal of ' experimental Wilson's disease ' have hitherto failed. From our standpoint the problem is not properly stated in either case. (1) In experiments no attention is paid to the great difference between the integrative levels of the nervous system in man and the animal respectively. Further, the question of *time* is overlooked; the speed at which certain biological phenomena unroll themselves and that (vastly greater) at which our grosser experimental surgical interventions take place, are utterly different. (2) Though it is customary to oppose to each other the two pathogenic alternatives—hepatic origin or cerebral origin—there is a third alternative which does not appear to have been considered. The presence of habitual emotional icterus leads us to ask whether our case is not one of primary disorder of a functional synergy (as in endocrinopathology) between subcortical organo-vegetative representations and the liver. On the one hand, as a matter of fact, the conditions of biological functioning of the liver depend on the organo-vegetative system; in respect of emotional icterus, it has been practically demonstrated by Eiger to depend on vagal hyperexcitation (vagus being used in its macroscopic anatomical sense). On the other hand it is proved that the normal functioning of the liver is necessary to the functioning of the organo-vegetative system (Danielopulu, 1931). In other words, it would appear that for the physical notion of *unilateral* causality must be substituted the biological idea of *reciprocal* causality. Emotional icterus appears to be the sign of a facilitation of vegetative nervous stimuli in a direction determined towards the liver, and we shall see later that in certain circumstances it is the same for the stomach, also innervated by the vagus. On the other hand, the instance of icterus neonatorum shows that biliary pigments and probably other substances as well can pass the hæmato-encephalic barrier (specially the choroid plexuses)

and reach paraventricular cerebral formations. This, needless to say, is no more than a hypothesis; none the less the notion of a primary affection of organo-vegetative representative centres seems singularly confirmed by the evolution of the syndrome in time. Let us recall its main lines.

VARIABILITY OF SYMPTOMS.

The most characteristic and most general feature is the variability of the symptoms. Whether they consist of muscular rigidity (see paragraphs 10, 12 above) sialorrhœa (12), dysphagia suddenly disappearing at a late stage of the disease (17, 26), bradyteleokinesis (19), volume of thyroid (22), general attitude of body (26), spasmodic weeping (32), especially the dysarthria (15, 23), the symptoms are in essence mobile and differ according to their period, so that we already get the idea (unless we are content with a fragment of the clinical picture artificially separated) not of a static disturbance (like an organic hemiplagia of vascular origin which has reached the residual stage of von Monakow), but a dynamic affection of a peculiar kind.

Further, a glance at the urinanalyses, conducted sometimes at intervals of only a few days, or at the blood examinations (of less demonstrative value), will reveal the same variability (though the alimentary regime was identical). We see, for instance, the total nitrogen pass from 7·89 to 12·80, Maillard's coefficient from 5·1 per cent. to 3·7 per cent., or the ratio of NaCl to urea pass from 100 per cent. to 81·5 per cent., whereas the normal figure is 42 per cent. The internal milieu, one of the essential components of the vegetative system in the sense of F. Kraus, characterised here in a rather crude fashion, we admit (it is impossible, according to Zondek, to have at present a complete intratissular representation of it) varies notably, even remarkably, in the course of time. Here is an evident dysregulation which laboratory methods, simple enough, are able to demonstrate. Thus the question is at once reached: What is this dysregulation, and does it bear any relation to the dysregulation immediately suggested to the mind by the variability of the symptoms?

RELATION OF SYMPTOMS TO LESIONS.

A preliminary remark must first be made. Some years before the War there were still writers who classed with the neuroses syndromes accompanying nervous lesions as obvious as those which concern us here. They relied both on precise observation—the occurrence of phenomena dubbed hysterical in such patients—and on a defective method which concealed simple ignorance by the use of a word. Real progress was attained by the method which succeeded it, at least to begin with. Legitimately proud of the acquisitions of anatomy (secondary degenerations) and of clinical medicine (precise semeiology of affections of pyramidal and cerebellar paths), neurologists have termed 'extrapyramidal' (a vague expression) everything that could not be classed in the other categories. Justifiably enough: but the method appears to have been imperfect when the neurologist has sought to assign to each symptom or

group of symptoms a strict and precise anatomical localisation: examples might be furnished from the literature of any country in the world. Such procedures have led to the development of the sophism denounced by von Monakow, which consists in identifying the localisation of lesions and of functions. From this viewpoint Wilson has submitted current interpretations, attributing a host of heterogeneous symptoms to the corpus striatum, to a most searching criticism in his Croonian Lectures of 1925, which, in our opinion, form a contribution destined to constitute a landmark in the neurological history of a type of disease which he was the first to study (1912) in a truly fundamental manner.

In point of fact it is only too evident to anyone who has in mind (1) the integration of motor function from the foetus to the adult, and (2) the emigration of function towards the superior surfaces of projection and association (Steiner and v. Monakow), that it is impossible to localise in the corpus striatum the automatism of movements (itself merely an abstraction) and akathisia! We wish now to go further and ask whether, apart from the mechanisms playing a genuine rôle in the pathogenesis of affections here considered (cortical, striate, rubral, cerebellar, mesencephalic components, and others), admirably studied by physiologists of the schools of Sherrington and Magnus, and by anatomo-clinicians, there is not room to pose the question of a more general factor, from the standpoint of biology as we shall define it.

THE BIOLOGICAL STANDPOINT.

We mean thereby not the study of such and such a function artificially isolated—which is the work of experimental physiology—but the study of the ensembles of phenomena having for their purpose not merely the conservation of the individual considered as a whole but also the realisation best adapted for all his potentialities. From this point of view the propulsive and at the same time regulatory force resides in the *vegetative system*. By that term we understand, after F. Kraus, not only the vegetative nervous system in the strict sense (sympathetic and parasympathetic), which plays a certain regulatory part, but also the electrolytes, among which calcium and potassium are the best known, the hormones, and the colloidal balance, local in the tissues. Probably many other components exist as well. From this standpoint Zwaardemaker has opened up wide perspectives through his admirable researches on the relations between the various radiations discovered by the physicists and the function of the vegetative nervous system. This is the conception of Kraus and Zondek, the only one at present capable of taking into account innumerable phenomena that cannot be interpreted by the 'classic' doctrine of Eppinger and Hess.

We owe to W. R. Hess of Zurich a very important contribution to the study of sleep conceived of as a biological process of defence of the organovegetative system (Hess in fact adopts the classical doctrine in this matter), guaranteeing the animal system against exhaustion. Recently the conception has been

extended by Hess, Foerster, Altenburger, Kroll and others to the function of the receptors, which are taken to be sheathed in a vegetative apparatus destined for the regulation of function.

If it really is so, if modifications of tonus and of static function during sleep are in correspondence with the vegetative system, why should it not be the same during waking life, so far as concerns the normal regulation of function of skeletal muscles and their dysregulation in the course of certain affections ? We think it is precisely so-called extrapyramidal syndromes (at least in some of their aspects) that are of a kind to confirm this way of looking at the matter.

Clinicians have always been struck by the frequency therein (one might say constancy if they were properly looked for) of undeniable vegetative disorders. In our case of Wilson's disease in the adult we note salivary trouble from beginning to end, as well as of lachrymal and sudatory secretions (16) ; disorder of thermal function (5) ; of cutaneous pigmentation (10, 15) ; of micturition and defæcation, throughout ; vasomotor disturbances (27) ; transient respiratory affection (21) ; transient thyroidal disorder (23) ; trophic change (25) ; and finally the ' vegetative death ' of L. R. Müller (32).

Again, in this category of patients symptoms reminiscent of hysteria have all along been remarked. Is it not a curious thing in our case (see 8) that the muscular rigidity reached the mid-thigh, recalling the stocking- or garter-anæsthesia of the classical hysteric, which has not always been the result of suggestion though thought to be so ? Above all, in this case observed during its evolution of seven years, what has impressed most has been the enormous variability of the symptoms, filling the entourage with astonishment and leading them to doubt my prognosis. This was particularly noticeable in regard to speech, which was often normal at the commencement of an interview and became dysarthric only after some minutes (15). Similarly, the dysphagia which had lasted for years (with some variations, it is true) disappeared completely for a fortnight (17, 26) ; likewise, the spasmodic crying vanished towards the end (32). The same changeableness affected muscular rigidity (10) and the secretions. The intensity of the dysuria and the dyschesia was also subject to variations, though they were the most persistent symptoms observed. Finally, the patient once presented complete disappearance of all his symptoms for 24 hours (6).

From all these facts of observation a profound difference may be noted from what occurs in the course of ' morphological disorders ' (v. Monakow and Mourgue) through lesions in continuity of nerve substance at a residual stage. If some youthful subjects of traumatic hemiplegia sometimes recover part of their movements, so far as I know a return to normal for 24 hours has never been observed. Facts of this kind have led authors to speak of neurosis, and of hysteria in particular.

The following facts, to which we attach some importance, must also be added ; their theoretical significance will be discussed later on. The patient

presented the bradyteleokinesis described by Schilder, for the first time, we believe, apropos epidemic encephalitis. Now by the aid of strong instinctive stimulations, in an imperious tone, the symptoms could be made to disappear rapidly (19). It was the same with dysphagia (25). We shall see that in these instances there is activation of the vegetative system, it having been shown that every psychical action of one person on another can be effected only by the intermediary of the instinctive or vegetative sphere.

FATIGABILITY.

We reach now what we consider the essential feature of our case : the rapid fatigability. It was general, and involved the dynamic as well as the static function of muscle, contrary to what Trousseau had formerly observed in the case of Parkinsonism (Dyleff, 1909). To be sure of this one has only to examine the electromyographic tracings of flexor communis digitorum (right and left) during the action consisting of compression of a rubber bulb for about one second, and those of the sural triceps (right and left) when the patient is on his toes (figs. 3—10). The first series (figs. 3—6) was taken after a rest of half an hour, in the recumbent position, the second (figs. 7—10) about two minutes later. The first tracings are normal, except for a slight tendency on the left side to fusion of excitations. Throughout it is seen that the left side (especially the left leg) is constantly more affected than the right. The second series show a set of biphasic oscillations, with a frequency of 24/27, characteristic of commencing muscle fatigue. Such is the interpretation given us by the late Prof. Wertheim-Salomonson, who had an opportunity of seeing the tracings taken by M. Bull in the Institut Marey using a string galvanometer of his own construction.

This extreme fatigability also involves another apparatus of the animal life, viz. the larynx. The methods of experimental phonetics, with the help of M. l'abbé Rousselot, of the Collège de France, have furnished exact information on the nature of the dysarthric disorders of our patient. The registering of laryngeal vibrations is made on a rapidly rotating cylinder with the help of the laryngographic capsule of l'abbé Rousselot. As he has explained to us, in the tracings (figs. 11 and 12), with two successive pronounciations of the same syllable the patient makes a great effort, so much so that the first is violent and acute, the second, on the contrary, is soft and trailing (to po, fig. 11). The patient's power of effort is largely exhausted on the first syllable. The fact is so definite that in this group of two syllables, forming for the French, in a way, one word, the accent is never on the final but always on the initial syllable. Further, when the repeated syllable commences with an occlusive, this consonant fails to lead to occlusion in the middle of the word, between the vowels, showing that the patient is almost incapable of making a sufficient effort to obtain this by complete closure of his mechanisms (té pé, fig. 12). To sum up in two words : extreme fatigability.

ELECTROMYOGRAPHIC TRACINGS TAKEN DURING REST.

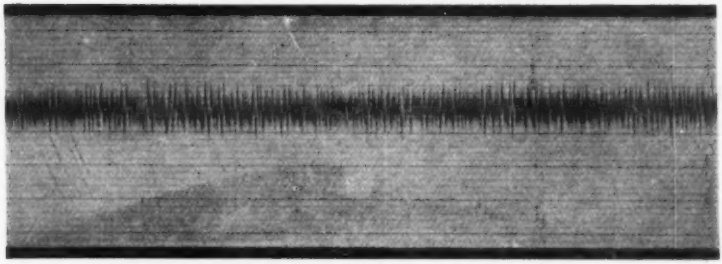


FIG. 3. Tracing of right flexor longus digitorum. Sustained contraction. Feb. 11, 1921

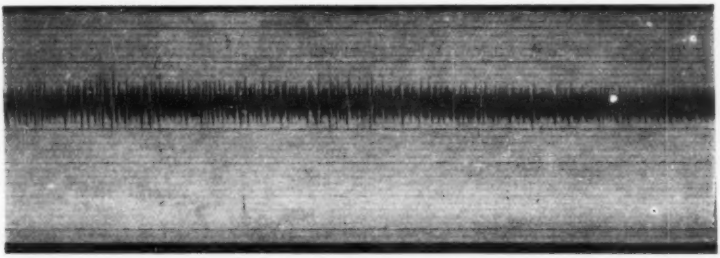


FIG. 4. Same muscle, left side.

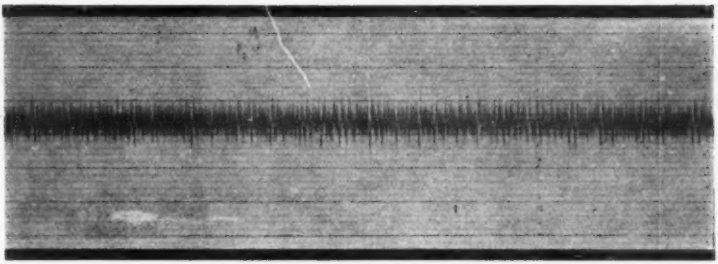


FIG. 5. Sustained contraction of right sural triceps (the patient being erect on his toes)

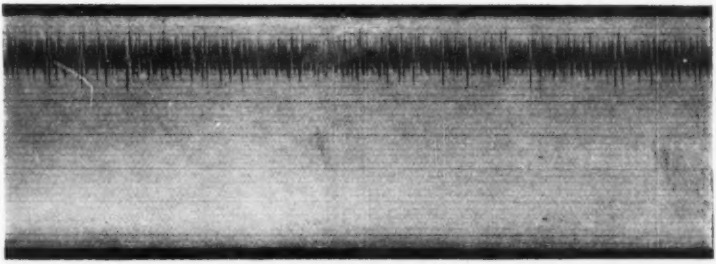
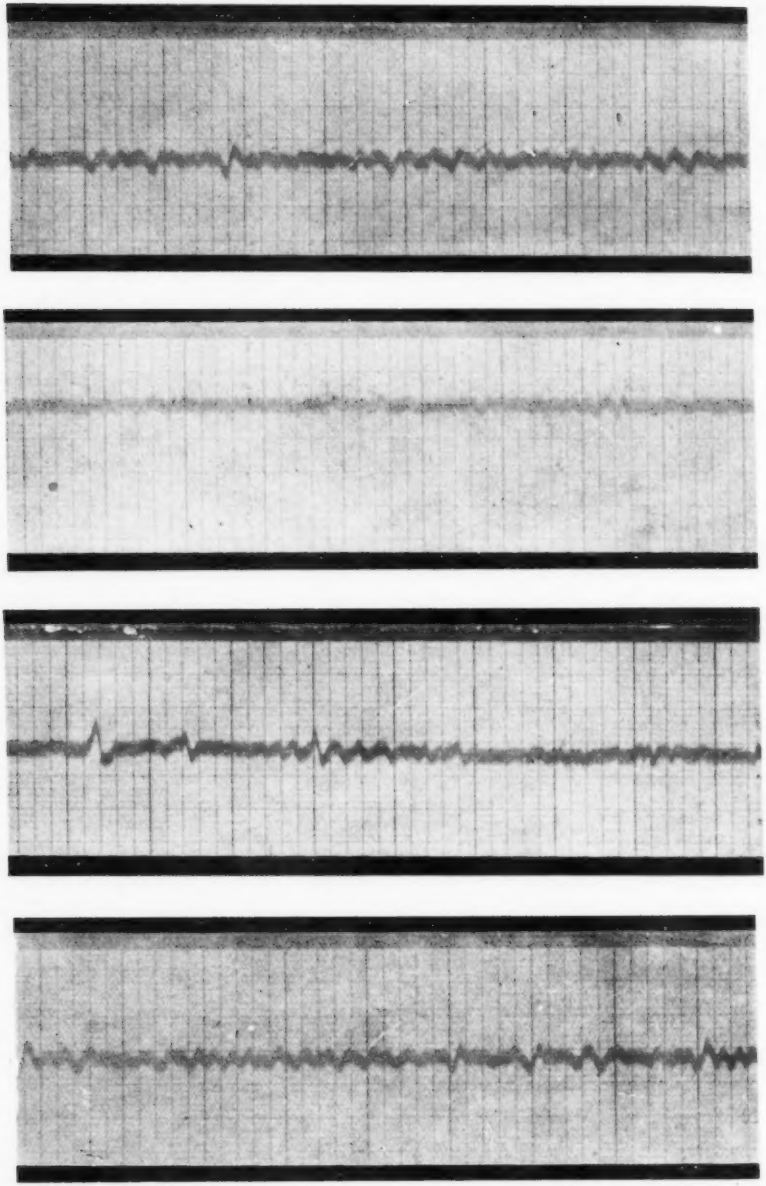


FIG. 6. Same muscle, left side.

ELECTROMYOGRAPHIC TRACINGS TAKEN TWO MINUTES AFTER THE PRECEDING.



FIGS. 7-10. Corresponding muscles to those of first series. Time intervals (vertical lines) 1/100 sec.

BIOLOGICAL MEANING OF THE SYMPTOMS.

What, now, is the biological meaning of the facts of observation just described ? For a long time it escaped us, which explains why we only decided to publish the clinical record and the protocol of part of our experimental researches several years after the death of the patient.

From what has been said, numerous facts of observation plead in favour of involvement of the organo-vegetative system ; in 1919, in a paper on ' The psychomotor function of inhibition studied in a case of Huntington's chorea,' we established experimentally the primary involvement of the central subcortical representation of the system, a point to which F. H. Levy indicated assent later (*Die Lehre vom Tonus und Bewegung*, 1923).

Up till the present, however, physiological findings to which the neurologist must submit himself were calculated rather to mislead than to inspire. It is

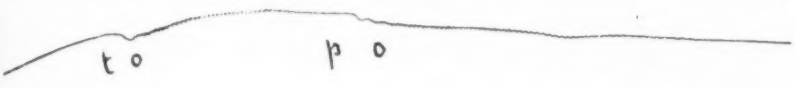


FIG. 11. Laryngeal vibrations during the pronunciation of 'to-po.' Time marked by tuning fork of 200 double vibrations a second. June, 1921.

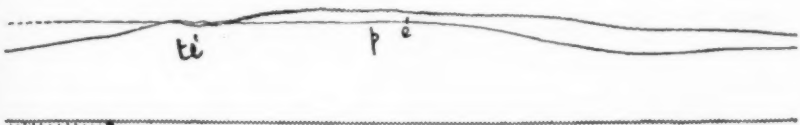


FIG. 12. Same as in fig. 11. Pronunciation of 'té-pé.' June, 1921.

not necessary for our purpose to enter into the complex question of the vegetative innervation of skeletal muscles. Although it has been anatomically established for certain muscles (Boeke), the views advanced by different authors (Bottazi, de Boer, Hunter, Langelaan and others) on the direct sympathetic regulation of muscular tonus have encountered too many experimental objections to be regarded as proved. Langley in particular showed the impossibility of accepting the plausible theory of Pekelharing according to which muscle tonus is accompanied not by a breaking up of carbohydrates but of proteins with formation of creatin.

In recent years the problem, obscured by the tenacity with which the abovementioned authors have regarded tonus and sympathetic as equivalent terms, has been entirely reshaped by the researches of the Russian physiologist Orbeli and by those of his pupils, who have shown that sympathetic stimulation

is capable of producing delay in the appearance of fatigue or a transient restitution of the capacity for work of a fatigued muscle. The tension of muscle during isometric tetanus can be augmented by sympathetic excitation. Fulton (*Muscular Contraction*, 1926) has recognised the solidity of Orbeli's work. His own tracings and those of Nakanishi show the reinforcement of tetanic contractions when, in addition to somatic nerves, sympathetic fibres are stimulated. These facts have been confirmed by the following negative data from Orbeli's laboratory. After unilateral extirpation of a sympathetic chain in the dog the reflexes of the limbs are profoundly altered. In eliciting rhythmically the patellar reflex, the limb deprived of its principal sympathetic connexion fatigues quicker and the reflex twitches are slower; similarly the reflex reactions to thermal and electrical stimuli—normally of the same threshold right and left—develop a threshold altogether asymmetrical after unilateral sympathetic extirpation.

Independently of the Russian physiologist, Achelis of Leipzig has been able to determine the influence of the sympathetic on the cerebrospinal nervous system. Starting with the important discovery of Lapicque, that the excitability of a peripheral nerve increases after separation from the spinal cord or ablation of the optic lobes (in the frog), Achelis has confirmed it and found in addition that interruption of conducting paths anywhere between eye and ventral spinal roots is followed by augmentation of peripheral nerve excitability. This signifies that in the normal frog (which Achelis studied) the excitability of peripheral nerves is inhibited by excitations of optic origin. Conversely, he proved that section of rami communicantes entails diminution of excitability of sciatic nerves. Hence one may conclude for increase of excitability of the peripheral motor neurone of sympathetic origin—and this, as we have seen, is entirely corroborated by the experiments of Orbeli.

All these researches have been repeated in animals bled to death; vasomotor effects can therefore definitely be excluded. Quite recently (1931) the views expressed by Orbeli have been confirmed by Altenburger and Weisz.

As can be seen, this conception of the rôle of the sympathetic strikingly confirms conceptions previously expressed by Hess, who, in his magistral study of the problem of sleep, originated the idea that the central nervous system of the animal life may be regarded as the effector organ of the organo-vegetative system. This theory is in complete accord with the primary rôle of instinct in nervous pathology as v. Monakow and I have explained.

To return to the problem of skeletal musculature, we see how much wider is the conception than that, calculated on our ideas of the nerves of the animal life, of tonic sympathetic nerves. Thanks to the admirable work of Sherrington and his pupils, during the last ten years, there is no longer any doubt that tonus (a term sanctioned by usage but defective) should be identified with the stretch-reflex. In Fulton's words: 'Stretch, therefore, appears to be the adequate stimulus for the maintenance of the tonic condition; in the stretch reflex

we have tonus in its making ' (p. 426). This is also the attitude of Rademaker, who in his fine book *Das Stehen* distinguishes several varieties of stretch-reflexes in accordance with the anatomical level involved. Tonus is a proprioceptive reflex, and the idea of a tonic sympathetic activity, conceived of in anti-physiological fashion as passing from a sympathetic ' centre ' to muscle, whereas every nervous activity constitutes a closed cycle (Morat), must be discarded. This does not mean—let it be well understood—that there can be no indirect connexion between tonus and the organo-vegetative system ; one has only to recall the modifications of tonus during sleep. Besides, there is not a single biological phenomenon, inclusive of the highest cerebral functions of man, which is not in connexion with the system ; it is in this general sense that tonic function, like phasic function, depends on the vegetative system. As a matter of fact it is to the theory of Kraus that adherence should be given for a clear view into the extraordinary complexity of the relations of the organic and the animal life.

ORGANO-VEGETATIVE SYSTEM.

If now, returning to the facts narrated above, we seek to interpret them, it is easy to perceive that they receive a new light from recent physiological advances. Two series of facts can be recognised : (1) a series of organo-vegetative phenomena (secretory disorders, metabolic and sphincteric disturbances, etc.) ; (2) a series of motor phenomena remarkable for their variability and specially distinguished by extreme fatigability. It is here convenient, before going further, to say a word on the limits of applicability of experimental physiology to clinical medicine.

(1) First of all there is the question of the physiological level involved. The lower this level is, the more general is the value of physiological data ; it is the case here, where the function is old from the viewpoint of phylogeny and ontogeny. (2) Physiological method requires the artificial isolation of function (decerebrate, mesencephalic, spinal, neuromuscular preparations, etc.). Pathology, which in certain circumstances can produce dissociations of which physiology is incapable, usually deals with gross and diffuse lesions (as in Wilson's disease) involving several functions at once. Besides, one must take into consideration the action of *diaschisis* at a distance (v. Monakow), as well as the processes of compensation and of effort for restitution of function, as we have ourselves worked out with v. Monakow. In our opinion, and it is true for both neurology and psychiatry, every syndrome is an aggregate of symptoms of which only some possess, in the present state of knowledge, a biological significance in the sense defined above. Thus, for instance, in our patient the exaggerated salivation, dysphagia, sphincter impairment cannot seemingly be ranged in the imbalance of the regulatory function of the vegetative system in its connexions with the animal system. They consist probably of derangements related to diffuse lesions of the periventricular grey matter. By contrast, the excessive fatigability and its variations seem properly to be a

phenomenon of the same order as those discovered by Orbeli. The fatigability recalls Addisonian adynamy ; in point of fact our patient showed pigmentation of the skin (though not of the mucosæ, while blood pressure was normal) as Söderbergh has also seen in a case of the kind.

It would be more than hazardous to incriminate here the sympathetic in the strict sense as the physiologists might do, in the first place because we have no incontestable criterion in human pathology of sympathetic deficiency, and above all because there is here an abstraction without reality. All that can be said is that it is highly probable that the conditions of existence of fatigability should be sought in the severe perturbations of the vegetative system (in the sense of Kraus) in our patient. As can be ascertained above, the classical pharmacodynamic tests, false in theory and practice (Söderbergh) furnish none of the information which one expected of them, not so long ago. Nor should it be forgotten that adrenalin and other drugs act particularly on the neuromuscular junction, the ' periterminal network ' of Boeke (Langley). In addition to the tremors with adrenalin it is interesting to note the nystagmus with atropin and scopolamine, which seems to indicate a susceptibility of the labyrinthine vegetative apparatus (Spiegel). On this subject we draw attention to the great variations in the size of the thyroid (23), variations which we have also observed in certain cases of disseminated sclerosis. Possibly these variations constitute a reactional phenomenon of compensation, if one allows (as seems well established) that one of the essential functions of the thyroid is sensibilisation of the vegetative system, especially of the sympathetic in the strict sense (Asher, 1931).

We must now add that if the vegetative apparatus can condition fatigability, inversely that apparatus is not independent of the animal system in its behaviour ; this shows once more the extreme complexity of the phenomena we are dealing with and the relativity of our divisions, which possess mainly a heuristic and provisional value. Here is an example. Up to recent years fatigue during static muscular exertion was considered to depend on the formation of lactic acid. This view can no longer be maintained since the studies of Dusser de Barenne and Burger, Zondek and Matakas, and others ; according to the first two of these, fatigue cannot be explained chemically (formation of lactic acid) nor mechanically (arrest or slowing of blood circulation) ; it can only be accounted for by the summation of *afferent excitations* (pressures and tensions to which the sensory neural terminations of skin and muscles are subjected). This hypothesis explains why fatigue does not appear in states of catatonia, catalepsy, or hypnosis.

Much earlier (1904) Féré had already proved by ergographic methods that all afferent stimuli (cutaneous, visual, auditory, etc.) are capable of producing fatigue, but neither he nor any subsequent author, so far as I know, has sought an interpretation of the phenomenon. Now it is very curious to note the state of affairs in our patient. At the period when the tracings were

taken, reproduced in figs. 13—16, we were surprised by a seemingly paradoxical feature. We took the graphs with the mercury column dynamograph of Charles Henri, right and left hand alternately, first in the erect and then in the recumbent position, the patient lying on a couch stuffed with hair. In both

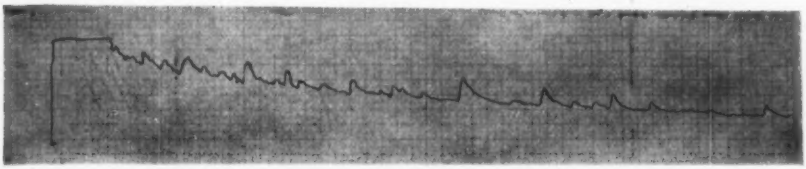


FIG. 13. Dynamogram (dynamograph of Ch. Henri) of the flexors of the right hand : standing position, slight anteroflexion of trunk. July 25, 1920.

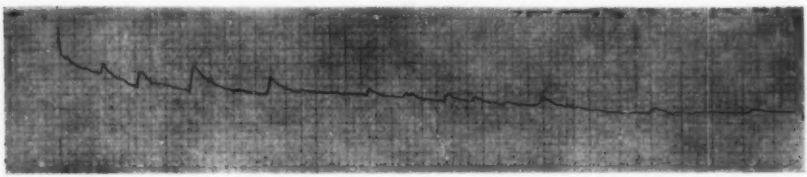


FIG. 14. Same as in fig. 13. Left hand. July 25, 1920.

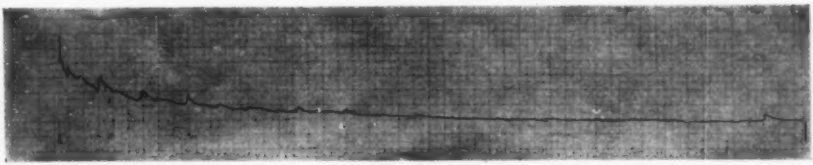


FIG. 15. Same as before. Right hand : position, lying down. July 25, 1920.

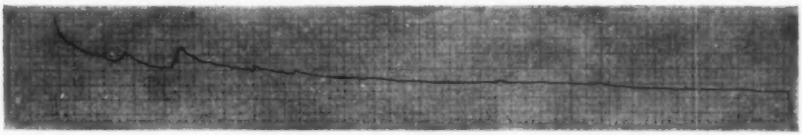


FIG. 16. Same as before. Left hand : position, lying down. July 25, 1920.

positions the patient employed not merely the flexors of fore- and upper arm, but also the muscles of the trunk and lower extremities. It may be recalled that the dynamograph works by means of manual compression of a rubber bulb filled with mercury communicating with a vertical tube similarly filled : each test was separated from the next by a repose of 25 minutes in a comfortable

chair. Examination of the tracings shows that in the erect position the output of work was superior to but less regular than that in the horizontal position. On the other hand, the patient affirmed categorically that he experienced less fatigue after tests in the latter position. This is the exact contrary to what I have been able to observe on myself and on normal subjects.

Such a result, it would appear, can be interpreted only in the sense indicated by Dusser de Barenne and Burger. In the lying-down position exteroceptive stimuli (plantar surface in particular) and proprioceptive stimuli (postural tonus in relation to antigravity function) are totally suppressed ; the nervous system of our patient was in such a state that he could only receive a limited number of afferent excitations without fatigue (a defence reaction) developing.

The question now arises : what is the terminus of these afferent stimulations ? Let it be said at once that the hypothesis of the organo-vegetative nervous system appears to be the most probable.

One of the most important principles of vegetative physiopathology, evidenced by Danielopolu, is to the effect that afferent impulses coming via centripetal visceral paths (as in angina pectoris), or via general sensory routes (as in the gastric crises of tabes) have a certain influence on the vegetative centres with which they enter into direct or indirect connexion. So far as concerns somatic muscles, not only are other afferent impulses than those from muscles (optic and auditory mechanisms) capable of causing fatigue (Féré), but, above all, proprioceptive and exteroceptive impulses (skin, articular and juxta-articular tissues) are susceptible of action on the central representations of the organo-vegetative system and of there producing modifications (still of unknown nature) provocative of fatigue. What is repose if it is not the more or less complete cessation of proprioceptive stimulations ?

What shows well that the essential part is played, not by products of muscle metabolism (which, for that matter, may excite afferent intramuscular terminals) but by the central condition, is the existence of fatigue persisting in the absence of all muscular labour. We shall make allusion to but a few of a whole series of facts. (1) Popular language has ever confirmed the rôle of the organo-vegetative system by such expressions as ' excitement has taken away the use of my arms and legs ' (Cannon would see there the consequence of a powerful suprarenal discharge) : or ' emotion has left me speechless ' (the *vox faucibus haesit* of the Latin poet). Some years ago we had under observation the case of a woman who after repeated emotional shocks developed an organo-vegetative dystonic syndrome with two predominant symptoms, viz. rapid fatigue, amounting in the end to unintelligibility, of the vocal cords when a given consonant was repeated, and the development of a husky voice about five in the evening (at the time of normal organo-vegetative change in the nycthemeral cycle) : also, about the same hour, fatigue of the arms with the slightest emotion, preventing her from holding a newspaper at the level of her face.

In our patient the fatigability of the phonetic muscular apparatus was altogether independent of that of the skeletal musculature. In amyostatic syndromes, therefore, fatigue cannot be ascribed uniquely to muscular work continually produced to maintain faulty static processes, as suggested by Froment in studies of much interest.

(2) We may cite here also the syndrome of muscular fatigue on an organo-vegetative basis seen in the Beard type of neurasthenia (the term is unsuitable for any other syndrome). We have had the chance of following for eight years continuously a case of this kind, connected probably with a 'plexitis' (hyper function of the choroid plexuses of the fourth ventricle), consecutive to trigeminal excitation of nasal origin. The case is too complex to be related here, but we may say that after minute study of each function by authoritative specialists we come by exclusion to the hypothesis indicated above, favoured also by v. Monakow. In this case, which presented a severe vegetative dystonia, it was curious to note the recurrence of fatigue coincident both with moderate muscular exertion and with emotion. In view of the dystonia all pharmacological therapeusis (purely theoretical at present) proved not only inefficacious but actually harmful, whereas a complete cure resulted from absolute rest and psychotherapy. It must not be forgotten that the phenomena with which we are here concerned have always a psychical aspect revealing itself clearly in the patient's dreams.

It may also be mentioned (we will return to the point) that the patient to whom we have just referred, only after severe fatigue and at a given moment, exhibited the *Randreflex* of v. Monakow, a form of plantar reflex common in mild degrees of pyramidal involvement. We do not think (we shall see later why) there was here any interruption of pyramidal fibres.

(3) Finally, it is known that one of the commonest symptoms of disseminated sclerosis (found in 90 per cent. by Sachs and Friedmann, 1922) is extreme fatigability coupled with muscle weakness and with others that need not be mentioned. It is also one of the most constant symptoms of the atypical cases of the affection, frequent now in the literature, and denominated diffuse encephalomyelitis. We have had an opportunity of observing a case with a peculiarity of interest in connexion with the present problem. It is that of a man of 35, wounded 15½ years ago by a bullet through the dorsal external border of the *left* foot, with exit towards the middle of the anterior part of the sole. Continual suppuration led to several curettings of bone. At the base of the second toe is an area of about the size of a two-franc piece in which originate excessively painful sensations of protopathic type to be inhibited only by firm pressure. For a year the *right* leg has been seized with violent tonico-clonic twitches whenever pressure is put on the anterior plantar surface of that limb. A sympathectomy was performed on the femoral artery (about 12 cm.) on the right, and the tonico-clonic movements, which interfered severely with walking, improved to the degree of rendering the latter

possible, although slight scratching of the sole still evokes a flexor contraction of the limb with clonico-tonic convulsions.

Simultaneously in this case unmistakable signs of disseminated sclerosis have made their appearance (cerebellar and labyrinthine signs, absent abdominal reflexes, nystagmus, etc.), together with considerable fatigability of the legs, which did not improve until the patient followed my advice and worked seated. One may ask whether the continual protopathic afferent impulses from the plantar surface of the left foot may not have been reflected, at the corresponding spinal level, (anterior and lateral horns) over to the contralateral leg. It is interesting to note that the sympathectomy appears to have acted as in the stump epilepsy of amputated limbs by suppression of a part of the afferent path.

And now, what is the bearing of this instance on our case of hepatolenticular syndrome ? As for connexions of the vegetative and the animal systems, it seems to us that, in disseminated sclerosis equally, muscle fatigability is a function of the former, if it is true that periventricular grey matter is practically always involved. We do not consider, naturally, that the lesion, a negative phenomenon, can explain the positive symptoms of fatigue; but the lesion is an index of regulatory defect which has its sphere of action elsewhere and which is, further, still unknown so far as its exact nature at this level is concerned.

DYSREGULATION OF THE NORMAL RELATIONS BETWEEN THE ORGANO-VEGETATIVE SYSTEM AND THE ANIMAL SYSTEM.

What is meant, in our case, by defect of regulation ? From numerous contemporary researches in the domain of experimental physiology (Sherrington and his school) and of clinical physiopathology (Head,Wilson, Walshe, v. Monakow, Mourgue, etc.) the essential problem of neurology is conceived to be one relating to the extremely complex laws of the circulation of neural influx. Even at the spinal level, most simplified by physiological technique, the organisation of reflexes in time corresponds to a purely functional scheme ; as Sherrington has recently said : ' The simplest spinal reflex thinks, so to say, in movements, not in muscles ' (1931).

From the standpoint of physiopathology, the studies of Wilson on chorea, as well as the experimental work of Minkowski, have shown clearly that certain syndromes called extrapyramidal can result from lesions at very different neural levels ; the symptoms themselves result from disorder of co-ordination between afferent and efferent impulses. This disorder shows itself in numerous modalities (false summations, reduplications, anticipations, viscosity, etc.) as we have shown along with v. Monakow.

Another characteristic instance is that of disseminated sclerosis. Is it not strange, from the standpoint of the old anatomo-clinical method, to note that this syndrome, whose lesions are even by definition diffuse, betrays itself by an ensemble of symptoms sufficiently constant to allow of diagnosis ?

The reason in our opinion is that the nature of the syndrome, as with those known as extrapyramidal, is different from disorders by interruption of continuity or congenital lack of neural tissue (' morphological disorders ' of v. Monakow and Mourgue). I hasten to add that the relationship indicated above was established for the first time (from a different point of view) by Wilson.

That author, in point of fact, sees the common ground of the two conditions to consist of the effect of toxins of undetermined nature. This is extremely probable ; but we think we can go further in the same direction. It is admitted to-day that the site of application of drugs and toxins alike is primarily the vegetative nervous system (Orr and Sturrock) ; only, for reasons still unknown, it is such and such a part of the vast system that is affected. In respect of the two groups of diseases mentioned above, pathological anatomy informs us that periventricular and subthalamic formations are involved : in these cases there always appears to be a chronic derangement of the regulation of neural influx. This was particularly noticeable in the case of our patient.

What lends support to this view is for example the appearance, on left plantar stimulation, of a contralateral clonus of the toe, and then of the homolateral foot (12). Ionic modifications of the internal milieu followed by modifications of nervous influx may here be recalled ; we noted above (19) how slight acceleration of respiration sufficed to provoke sometimes a severe tremor of the right toes and then a spontaneous fan-like extension, sometimes extension of the last four toes on the right, left great toe, and trembling of the former. We know from the conception of v. Monakow that the extensor plantar response corresponds to a fixed change in the ordinary course of neural influx : nothing however here authorises us to associate it with interruption of pyramidal fibres, of which there is no evidence by classical tests. To speak in these cases of a latent pyramidal lesion is a petitio principii due to crude ideas of nervous function. Babinski's sign is found during the epileptic attack and in sleep.

On this matter we wish to direct attention not merely to the defect of regulation in the sense that the neural influx takes wrong routes but also that it persists sometimes in normal paths longer than is habitual with normal persons. After urination it is common to experience a brief shiver in skeletal muscles analogous to what obtains in fevers or accompanying a sudden chill (in both cases, organo-vegetative phenomena) : it is just as though proprioceptivity emanating from the tonic contraction of the vesical sphincter irradiates through skeletal muscles. In our patient, at an advanced stage, micturition, especially at night, was accompanied by attacks of generalised trembling (26).

Whatever be the opinion on the existence of vegetative fibres of ' tonic function,' we can rely on the active interrelation of the vegetative and animal systems. It is unnecessary to appeal to any special innervation. Renner

(in Müller's treatise on the organo-vegetative system) says a cortical bladder centre is more than doubtful; whereas the researches of Karplus and Kreidl show the possibility of influencing the vesical sphincter from the regio subthalamica, a region which forms, so to speak, a reservoir of nervous energy. There is thus nothing remarkable, in a case of dysregulation, in the accompaniment of vesical proprioceptivity by violent irradiations to the skeletal muscles. The neighbouring sphere, the genital, present a similar phenomenon: modifications of muscle tonus in skeletal muscles accompany the orgasm. Unfortunately in our patient libido sexualis was completely abolished, so that we can add no observations in this matter.

Two other facts of observation should in our view be interpreted as indicating derangement in the circulation of neural influx. These are the facial paresis of supranuclear type (11), which, having undergone remission, can only be assigned to a phenomenon of diaschisis; and the hemiplegic attitude noted at one time (19). It should not be forgotten that the patient never exhibited any of the signs regarded to-day as proof of anatomical interruption at any point in the pyramidal tract. Just as irradiation phenomena are a sign of

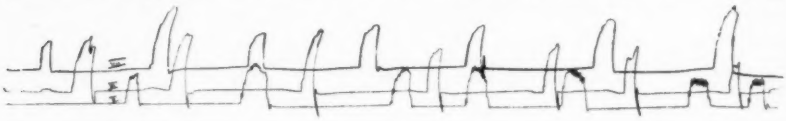


FIG. 17. Myograms of the extensor communis of toes. Faradic excitation, 14 interruptions per second. V = Right. VI and VII = Left. Time marked in fifths of a second.

disintegration resembling fragments seen in the new-born, so the hemiplegic attitude seems to correspond to predominance of the biceps, which according to Minkowski is a fœtal characteristic attitude. We have seen the same thing in a typical Parkinsonian case in a woman of 64.

Finally we may ask whether in one respect at least the hypertonus of the left side, especially in the leg, may be, if not caused, at least reinforced by the vegetative system. We underline the reservation intentionally, *if not caused, at least reinforced*, because as we have seen the proprioceptive origin of tonus can no longer be demonstrated. None the less proprioceptivity does not allow us to interpret the arrest of muscle tonus about five centimetres above the knee in the left leg. We have had the good luck to observe, in the case of Parkinsonism alluded to above, the same phenomenon on the left side but accompanied by trophœdema and paræsthesiæ (in intimate relation to vasomotor disturbance, according to Wilson), the whole extending to some five or six centimetres above the knee. The trophœdema leaves no doubt of their organo-vegetative origin. It was absent in the case forming our study, but the hypertonia thus localised was subject to variation from time to time. We established its genuineness by relying on the work of Wertheim-Salomonson,

FIG. 18. Tapping test. Time marked in fifths of a second. From below up:
1. Normal subject: right middle finger. 2. Patient: right middle finger.
3. Normal subject: left middle finger. 4. Patient: left middle finger.

according to which faradic tetanus is obtained in hypertonic muscles with a much weaker current than in normal muscles. His tracings from a case of disseminated sclerosis are quite demonstrative; no less are ours (fig. 17), in which the lower tracing is that of the right extensor communis of toes, the two upper representing the faradic tetanus of the same muscle of the left leg, with the same interruption of 14 per second. For normal muscles the average figure is 20, according to Wertheim-Salomonson. In the upper limb we have given another illustration of hypertonus, calculated to show the influence of tonic on phasic activity (which follow each other as the shadow does the body)

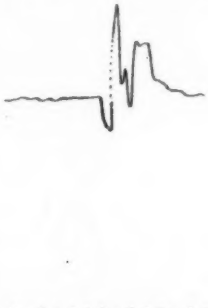


Fig. 19. Knee-jerk : right leg. Time marked in fifths of a second. July 7, 1920.

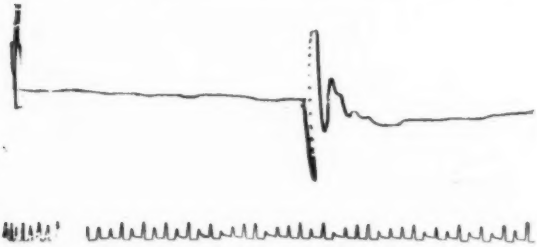


Fig. 20. Knee jerk : right leg. Same time. April 18, 1921.

by the help of the tapping test. This consists in making rhythmic percussion on a rubber ball connected with a Marey's capsule. The slowness and irregularity of the movement compared with the right side, and with that of a normal person, can be seen in fig. 18. But it cannot be too often repeated that these results are valid *only for a given moment in time*. The graph of the normal knee-jerk reveals the existence of two components, one tonic and one clonic (Piéron, Wertheim-Salomonson, and others). In accordance with the predominance of one or other we speak of hypertonus or no hypertonus. A glance at the figures will show that the same right side at one time exhibits predominance of the tonic component (fig. 19), at another of the clonic (fig. 20),

conformably to the moment of time ; on the left, incontestably hypertonic for the greater part of the time, a transient predominance of the clonic element is seen (fig. 21), when relative hypertonus has passed to the right.

Thus it may be questioned whether in extrapyramidal affections tonic phenomena are not complicated by secondary effects of organo-vegetative origin, deforming them more or less, and rendering them the least suitable affection for examination of tonus in a 'pure state.' At any rate, a hypertonia to the mid-level of the thigh is an altogether peculiar phenomenon. It should be remembered that vegetative phenomena are a function not merely of regulation of the vegetative nervous system but also of the local cellular condition. With the schematism inherent in our habits of mind we speak in current parlance of skeletal muscles, yet we know from the work of Schiefferdecker and Prenant that, histologically considered, 'the diversity of morphological characters, and their variation when one animal species is compared with another, suggest that each muscle, perhaps each muscle fibre, has its own

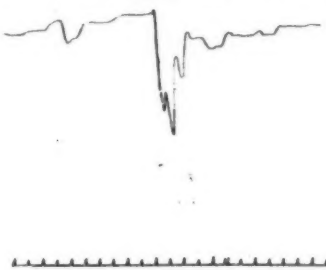


FIG. 21. Knee-jerk : left leg. Same time. July 7, 1920.

specific constitution, its own functional structure' (Prenant). Given this polymorphism, which my chief, the anatomist Vialleton, equally admitted, it is possible that the local electrolytic constitution, to which Zondek attaches so much importance as a component of the vegetative system, may, in the course of disorders like hepato-lenticular syndromes, profoundly affecting metabolism, differ at different spots in the same muscle. In this way would be explained both the inconstancy and variability of pharmacodynamic action, and the apparent paradox of irregular topographical distribution of the hypertonicity.

MIMIC AND EMOTIONAL SYMPTOMS.

We have not yet spoken of another group of symptoms in our case which may also be regarded as an aspect of maladaptation of the normal relations between the vegetative and the animal spheres. We allude, on the one hand, to the disappearance of facial mimicry (fixity of expression) and, on the other, to spasmodic weeping. The problem has been handled in a striking way from

the anatomo-clinical side by Wilson in his *Modern Problems of Neurology*. He relies on researches of Spencer and Graham Brown in attaching great significance to the facio-respiratory synkinesis during laughing and crying, and also to the existence of cortico-bulbar paths passing by the mesial part of the subthalamic zone bordering on the walls of the third ventricle and the tegmentum. In these conditions spasmodic laughing and crying are taken to be a phenomenon of escape of control, or of isolation in the sense used by Munk (Wilson does not employ the latter expression).

In support of these views, we may point out that (1) in syndromes designated extrapyramidal the lesions, as a matter of fact, predominate in the regions

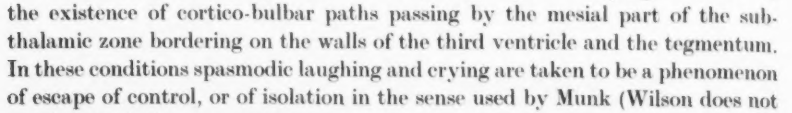


FIG. 22. Pneumograms. Instinctive reactions. July 17, 1920. Time: fifths of a second. Speed of cylinder: one revolution per minute.
Down curves = inspiration. Up curves = expiration.
1. Violent and unexpected auditory stimulus.
2. Another, less loud.
3. Slight prick of left shoulder.
4. Spray of ethyl chloride, posterior aspect, left arm.
5. Spontaneous transient apnœa.
6. 'I am sure you will be cured.'
7. 'Your disease is very serious.'
8. 'You remember your nephew killed in the war?'
9. 'Think of your nephew.'
10. 'Think nothing more of it.'

where the above-mentioned paths run; and (2) it is actually the case, in our patient, that to mimic facial inertia corresponds a diminution in the 'voluntary' power of respiratory acceleration.

All this is exact, we believe, but yet constitutes, we consider, only the *mechanical* side of the question, so to say; it does not give us the *biological* significance. As with the problem of sleep, knowledge of the local changes found does not provide the key to its meaning, as Hess has well recognised.

Some dozen years ago (1919) I was able to show experimentally, in a case of Huntington's chorea, using as tests plethysmography of the hand and graphic inscription of respiratory movements (a most delicate test, as Ponzo has shown), that such a case did not react to stimuli capable of evoking in the

normal subject active respiratory derangements emotional in nature. Yet the same patient exhibited attacks of violent rage of an automatic kind, since they supervened in the absence of any external stimulus.

Now the case is practically the same with our patient here. If one looks at fig. 22 and its legend, it will be seen he reacts only in a feeble manner (as compared with the normal) to sensitivo-sensorial excitations : this is true also of psychical stimuli, intentionally chosen from among those capable, as we know, of provoking strong reactions in the sphere of instinct. The attack of spasmodic crying at the end of the graph (to the right and above) need cause no confusion, in the first place because of its late development and in the second because a similar excitation (see 8) was not followed by any effect. Besides, the patient himself said that the attack of weeping had arisen in an unexpected way, as he had not been able to obey the order given. Similar experiments were repeated with the psycho-galvanic test and yielded the same results.

At the commencement of our observation the patient made it clear that from a subjective viewpoint (which must not be ignored) spasmodic weeping corresponded to something quite different from normal weeping. We may recall his own words : ' when I weep for sorrow, I sob ; when I weep as I have just been doing, it is not the same thing. When I weep for sorrow, I feel it comes from the heart ; when I weep like this, it is in spite of myself ; I feel it comes from the stomach. When I am sympathised with, all at once I am compelled to cry ; when I experience joy, I also have the inclination to cry. When I weep, I feel as I were being gripped (indicating the epigastrium) ; it is very hard to explain what I feel. It seems as if my stomach were shrivelling, and that ends with pains.'

According to this statement, it would appear that the patient shows at a given moment both forms of emotional expression, the normal and the spasmodic. According to his wife's information this is only true of the earlier years of the disease, and even then he seemed usually indifferent to happenings which would normally have aroused his emotions. We have been able to photograph the patient at a time when he said he felt a vivid emotion of annoyance (after an argument with his wife) supervening just when we were arranging to photograph the hemiplegic attitude of the left arm. The expression of his physiognomy at these successive moments is exactly the same, the more so as such patients have no difficulty in preserving complete immobility (fourth year of the affection).

To another fact we attach great importance, one often mentioned by the patient (see 16 in particular) ; at the moment of a spasmodic crying attack he is conscious of a particularly painful feeling of shrivelling in the epigastrium, which he has difficulty in describing exactly. We then wondered whether it was not a contraction of the gastric wall of vagal origin. We found this to be the case with the aid of the radioscopic screen (with the help of M. Contre-

moulins, radiologist to the Necker hospital in Paris). After ingestion of a bismuth meal it was easy to provoke the spasmodic weeping and to observe slow but definite contractions of the stomach. Everything points to vagal discharge at the moment of the weeping attack. This merely appears to be an exaggeration of a normal phenomenon; as was emphasised by van Helmont even in the eighteenth century, the stomach reacts most delicately to all emotions (cf. also Pavlov), and after depressive emotions the organ is 'fermé,' as a popular French expression has it. In our case this protopathic sensation had the strange, indefinable tonality characteristic of organo-vegetative phenomena of isolation (Munk).

How may the biological significance of spasmodic weeping be made to fit in, in our case? To do this it is necessary to pose first the more general question of the significance of what are called in classical psychology the 'physiological concomitants of emotion.' It cannot be here treated in extenso; we shall content ourselves by stating that we adhere to the view sustained by v. Wyss, a pupil of Hess, which declares that visceral reactions taken as a whole should be considered 'means of expression' (Ausdrucksmittel). This conception lends support to the views of Wilson on the respiratory synkinesis already alluded to.

What are these 'means of expression'? Von Wyss, after Sherrington ('emotion moves us, hence the word') and Klages take them as the mode in which the organism expresses by its attitude the instinct of interest in its connexion with the object (tendency to 'klisis' or 'ekklisis'). We add that in the circumstances the instinct utilises the skeletal muscles, a particularly important point. As a matter of fact we have here, at a somewhat low level, a manifestation of that connexion of the vegetative with the animal life which seems to us profoundly disarranged at that level in extrapyramidal syndromes. Our graphs provide the evidence for a hiatus between sensorial perception and effector organs; on the other hand, in spasmodic weeping, the latter come into play with the participation of exteroceptivity. Naturally the moment of time must never be omitted; at a certain stage of evolution normal mechanisms may still come into action at one time or another. It is not then paradoxical to admit that the 'fixed expression' is fundamentally a disorder of the same nature as fatigue, if we interpret the latter as has here been done. Thus the biological point of view, which since 1912 we have contrasted in superiority with the synthetic (after analysis) point of view, allows a unification of symptoms and a more profound comprehension of pathological processes.

METABOLIC DISORDERS.

Can we now go further and combine in the same formula even the metabolic disturbances making hepato-lenticular syndromes and the majority of extrapyramidal troubles following epidemic encephalitis affections of a fatal kind in a restricted time? We have already alluded to the 'vegetative death' to

which these patients succumb. Like general paralytics before malaria Therapy, like some juvenile catatonics, such patients reach a stage of extreme cachexia ; to them applies perfectly the expression formerly introduced by Edinger (though in another sense) of 'disease by exhaustion' (Aufbrauchkrankheit). Verworn has argued that cellular life depends on the formula $\frac{A}{D}$ where A= assimilation, D=disassimilation, and which he calls *biotonus* ; on condition that reserves are made, in agreement with Kraus, it might be replaced by $\frac{P}{S}$, where P=parasympathetic, S=sympathetic, the first system furnishing the necessary energy for the second, which expends it essentially by the intermediary of the phasic function of skeletal muscles.

It certainly seems that extrapyramidal syndromes terminating by rapid cachexia are signalised by the excessive predominance of the factor S, the sympathetic. Only, instead of the principal expenditure of energy involving phasic function, in its normal connexions with the external world, it would appear that without furnishing work the cell exhausts its reserves on the spot, so to say. Here is a process analogous to cellular autolysis, of which we know practically nothing.

But, as we have just said, the process seems to conduct itself, also as previously indicated, in the sense of a rupture of normal relations between vegetative and animal life. The vegetative system no longer holds at the disposition of skeletal muscles the amount of energy for their needs (hence fatigue), and as tonic proprioceptive function is already disordered a highly complex picture results whose variability is chiefly in relation with that of the vegetative system and which, in our opinion, forms the picture of the affections known as extrapyramidal.

CONCLUSIONS.

We should like to repeat again what was stressed at the outset, viz. that we have no intention of dealing here with disorders of tonus properly so called, but with the biological significance of extrapyramidal affections considered as a whole. It is convenient now to summarise what has been remarked in the preceding pages on this subject.

In our *Introduction biologique* (with v. Monakow) we distinguished rather schematically two main varieties of pathological disorder : (1) *morphological disorder* by interruption of continuity or congenital absence of neural tissue ; and (2) *secretory disorder*, which is the manifestation of derangement in the instinctive sphere. In the latter we distinguished diverse modalities, characterised by the examples of hysteria on the one hand and schizophrenia on the other, but we took the precaution of remarking that there are certainly others still (l.c., p. 313). If one admits (as we did with v. Monakow) that the whole life of the nervous system, under normal and pathological conditions, is dominated by the difference and interaction between two spheres (vegetative life and animal life, or, as we called them, sphere of instinct and sphere of orientation

and causality), one can perfectly understand the multiplicity of relations which may exist in man by reason of the degree of complexity which both spheres may attain. Thus there is no morphological disorder which may not be influenced in its behaviour by the vegetative or instinctive sphere. We may go further and affirm that every morphological affection has for correlate a disturbance of behaviour called psychical, which requires to be studied by appropriate methods (psychoanalysis in particular). We need not enlarge on this point, but we have indicated above (2, 30) the abnormal nature of the dream life of our patient.

We do not wish to insist on this, but rather on the fact that in the large group of secretory disorders the level involved must be specified. (1) From this standpoint we may put on one side *pyramidal* affections in their residual phase as constituting a class of morphological disturbances involving in almost pure fashion (in their circumscribed forms) the animal life at a high level, e.g. movements of dexterity, and leaving, almost intact, locomotion as a crude phenomenon. (2) Affections schematically designated *extrapyramidal* imply, as we have tried to show, rupture of normal equilibrium existing at different levels between the animal and vegetative spheres, the former considered principally but not solely at the postural level, since neural corticomotor regulation is also greatly disordered, as Wilson has shown. (3) *Psychoneurotic* motor affections constitute expressions of instinctive origin, organo-vegetative life being taken as the representative of instinct, either exclusive (' hormétéres ' or primary instincts), or partial, in connexion with the sphere of orientation and causality (' noohormétéres ' or elaborated instincts). The reader is referred to our book (with v. Monakow) for details of the conception : but we may add now that the animal life is involved at a much higher level than in the course of extrapyramidal syndromes, and that is, the ensemble of the cortex. At this level motor disorders have in man a symbolic significance. The experimental work of Hess and of Pavlov, though undertaken for different ends, harmonises in proving the process to involve the regulation of nervous influx. We may merely add that these processes can be effected by either the psychical or the physiological route—to employ the usual terms, absolutely vicious though they are ; we showed in the work already quoted that in both instances an action is effected on the vegetative system, a true ' common path ' (Sherrington). (4) Finally, *psychotic* disorder appears to differ from the preceding only by the extent and modality of the rupture of equilibrium at a very high level. that of the ' noohormétéres.' Psychomotor phenomena there present themselves not as disorders of movement but as phenomena of expression (Ausdruckbewegungen), symbolic of the primary derangement of the instinctive sphere.

We may add that these distinctions are purely schematic and rather abstract, seeing that all the phenomena of disintegration are subject to the law of disintegration ' en briques.' The following examples illustrate the

point. (1) Extrapyramidal disorders, if they supervene in persons who have in the past (sometimes in infancy) undergone a severe traumatism in the instinctive sphere, are complicated by unmistakable psychoneurotic disorders. Thus in the cases of oculogyric crises we have seen in postencephalitics we have nearly always been able to find evidence of old traumatisms involving the sexual instinct ; occasionally the symbolic character of the act of looking up is conscious on the patient's part, without any interference of suggestion. Jelliffe has written an excellent study on this, apropos attacks of tachypnœa. One may question whether any case of extrapyramidal disorder is unassociated with psychoneurotic symptoms. Every interruption of continuity between the sphere of exteroceptivity elaborated by causality and the instinctive sphere has always, more or less, for consequence a regression to the narcissistic stage of Freud, whence the door opens for psychoneurosis. One may here see the richness of the aspect from which we have sought to interpret extrapyramidal affections. (2) Motor disorder of extrapyramidal type is so little rare in the course of psychoses that special studies have been devoted to it (Schilder, Steck, and others). We do not range in this category schizophrenic catatonia, which is different in nature from the toxic phenomena superfically resembling it (v. Monakow and Mourgue, Claude and Baruk). Toulouse, who has had wide experience in examining psychoses at their apparent beginning, has found among the prodromes one presenting itself with singular constancy, viz. fatigability. Much taken up with the early unrolling of psychotic disorders, he has concluded—prematurely, as we think—that one of the tasks of mental prophylaxis is to discover objective tests revealing this tendency to fatigue. Several of his collaborators have undertaken researches in this connexion, mainly of a chemical kind ; in spite of their value so far as analysis of accompanying phenomena is concerned, we think the question wrongly conceived. As we have shown, fatigue appears to be an index of dysregulation supervening in the relations of the vegetative and the animal life, its starting place being in the vegetative system.

We should not forget that only on the occasion of interaction of the two spheres is fatigue felt ; it is always located in the interior of the animal sphere though having its real origin elsewhere. There is in reality no fatigue, in the strict sense, of vegetative visceral functions. It appears to be the economic reaction of defence calculated to protect the living organism against exhaustion and to prevent it from expending energy in favour of animal functions to the detriment of the conservation of life. In this sense it is a manifestation of the instinct of preservation at a low level. Hence it does not astonish that fatigue should occur at the onset of psychoses, since these have their origin in the world of instincts in close connexion with the vegetative life. It is only a sign, like fever.

We cannot at present determine many points which are still obscure. One of the most difficult, on which we have but a fitful light, is the existence

of a *chronogenic localisation* in the vegetative nervous system, like what obtains in the cerebrospinal nervous system (Semon and v. Monakow). Nevertheless researches such as those of Claude and Baruk, to which we draw attention, tend to produce a reaction against the simplistic views still reigning in the minds of some neurologists. The same movement is showing itself in different countries. We think this provides verification of the necessity of posing problems in biological terms, as we have defined the term, and that we have not been in error in urging for the last twenty years the insufficiency of the analytic point of view in biology.

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PROGRESSIVE HYPERTROPHIC POLYNEURITIS.

By

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This rare disease was first recognised as an entity by Dejerine and Sottas in 1893, four years after Gombault and Mallet had recorded a characteristic example, the true nature of which was not realised, under the title of "A case of tabes occurring in infancy." Since then a number of papers on the subject have been written, particularly by French authors, and cases have recently been reported by Slauck, von Mellin and others.

Progressive hypertrophic polyneuritis is a disease which may be manifest at any age and is often familial. The main feature is thickening of the peripheral nerves, which are often palpable and which present characteristic histological changes. There is muscular atrophy of the feet or hands, or of both, but it is usually more marked in the feet. The condition tends to be progressive and the muscles of the proximal parts of the limbs may be affected later. Deformities frequently arise, of which pes cavus, claw-hand and kyphoscoliosis are the most common. Diminution or absence of the tendon reflexes is the rule and sensory changes are not infrequent.

French authors have endeavoured to classify the disease into types.

Type 1. (Gombault-Dejerine.)—Characterised by muscular atrophy of the extremities, most marked in the distal parts, commencing and predominating in the lower limbs, accompanied by fibrillary twitchings and disturbances of the electrical reactions. Nystagmus and marked kyphoscoliosis are present and what may be described as tabetic signs, viz., lightning pains, anæsthesia of varying degree, Romberg's sign, Argyll Robertson pupils and absent tendon-jerks.

Type 2. (Pierre Marie-Boveri.)—In this variety similar muscular atrophy of the limbs is present without fibrillary twitchings, motor incoordination, Romberg's sign, Argyll Robertson pupils or nystagmus. The tendon-jerks, however, are absent and marked kyphoscoliosis, intention tremor and scanning speech occur.

Type 3. (Roussy-Cornil.)—This form is distinguished by being non-familial and commencing in adult life.

A number of cases may be placed in these groups but others have been observed which show wide variations, and many authors have not followed the above classification. In any case a fourth type must be included if the classification is to approach completeness.

Type 4. Harris and Newcomb, Nattrass and other writers have recorded cases of recurrent attacks of interstitial hypertrophic neuritis in which the nerves have shown similar histological appearances to those which occur in the other varieties of the condition.

Harris and Newcomb's case was non-familial and occurred in a male, aged 52, who had recurrent attacks of paralysis during six years. The signs and symptoms included weakness of the legs, bilateral foot-drop, wasting of the intrinsic muscles of the hand and some degree of anæsthesia. The knee-jerks arm-jerks, abdominal and plantar reflexes were absent and the affected muscles showed R.D. Their conclusion is expressed as follows: "It seems that the Dejerine-Sottas type of familial hypertrophic interstitial neuritis should be distinguished as a separate group from recurrent polyneuritis, to which our case appears to belong, though the interstitial hypertrophic neuritis found in the nerve-trunks and spinal nerve-roots in our case forms a remarkable link between the two groups, and it is conceivable that a similar underlying cause may be responsible for all of them, an auto-toxæmia such as is the probable cause of hæmatoporphyrinuric neuritis."

CHARACTERISTICS OF THE DISEASE.

Age and mode of onset.—In the majority of cases the onset of the disease is first noticed by the development of pes cavus in childhood; later, focal atrophy of the muscles of the feet and legs is present; wasting of the intrinsic muscles of the hands generally occurs after an interval of some years. Occasionally the first signs are not observed until adult life when the hands may be first affected.

Yokomori recorded the cases of a father and son in the former of whom the symptoms appeared at the age of 44 and in the latter at 26. Dide and Courjon reported five cases in 1919 and claimed that they represented a type of the condition not previously described. All their cases occurred in adults between the ages of 30 and 40: the muscles of the hands only were affected in all except two in which pes cavus was also present. The tendon reflexes were normal, the median and ulnar nerves are stated to have been thickened but there was no sensory loss. No pathological examination was made and in its absence and in view of the atypical nature of the cases it is doubtful whether they can be included as examples of progressive hypertrophic neuritis (cf. de Bruyn and Stern).

Heredity.—Heredity plays an important part in the incidence of the malady, although a number of sporadic cases have appeared, as may happen in other hereditary and familial conditions, e.g. Friedreich's ataxia, peroneal muscular atrophy and congenital cystic disease. A family history is obtainable, however, in almost all the cases in which the symptoms are present in childhood but less frequently when the condition has commenced in the adult.

Muscular atrophy and deformities.—The typical appearances are atrophy of the muscles of the feet and intrinsic muscles of the hands; as the disease

progresses the muscles of the legs and forearms may also be involved. The muscular atrophy, therefore, is distal. Fibrillary twitchings commonly occur. Associated with this muscular atrophy are the deformities generally described as claw-hand and club-foot. Hyperextension at the metatarso-phalangeal and acute flexion at the interphalangeal joints frequently renders it impossible to determine with accuracy the nature of the plantar response if it is present. Equinovarus deformity is sometimes seen. Kyphoscoliosis is of common occurrence and may be very pronounced.

Reflexes.—In all the cases described the tendon reflexes are either very markedly diminished or entirely absent. There are few references to the abdominal reflexes but in one of Russell and Garland's cases they were absent and in another they were sluggish. In the present series they were abolished in Case 1 but brisk in the others. These patients with absent abdominal reflexes were all adults in whom the disease had been present for some years and it is probable that this is a later development of the condition. On the other hand absence or diminution of the tendon reflexes occurs at an early age and may be found before any muscular atrophy or deformities are noticed (Case 3 in present series).

The plantar responses vary. In the majority of cases they are absent. In three of Russell and Garland's cases they are stated to have been flexor and in one definitely extensor.

Sensory disturbances.—These vary considerably. In a few instances no sensory loss has been detected; in others it has been well marked and of the glove and stocking variety, light touch being lost, sensibility to pain and temperature blunted and sense of position impaired. These changes tend to occur later in life and are progressive.

Pains in the limbs of lightning character are not uncommon. Vasomotor disturbances such as sweating of the hands and feet may occur and were present in Russell and Garland's first case and in Case 1 of this series.

Electrical reactions.—There has been some change in the electrical reactions in the majority of cases in which these reactions were tested. Most commonly there is no response to faradism in the affected muscles or the response is very sluggish. The response to galvanism is also sluggish. Changes in the electrical reactions probably occur late in life and become more marked as the disease progresses. They may be absent in childhood.

Cerebellar signs.—Nystagmus is referred to in a number of cases but does not appear to be a marked or characteristic feature of the disease. Intention-tremor is mentioned by Marie, and some clumsiness and incoordination of movement may be present: this, however, is probably not greater than can be accounted for by muscular weakness and peripheral sensory loss. Scanning speech was present in one of the original cases described by Dejerine and Sottas and in one by Marie but does not appear to be common.

Pupil reactions.—In three cases the pupillary reactions are stated to have

been sluggish or of the Argyll Robertson variety, but in the majority they are normal. Changes in the optic discs are not described and clinically the cranial nerves are unaffected, but Dejerine and Thomas state that both the cranial nerves and the cervical sympathetic are increased in volume. Marie and Bertrand also noted enlargement of the cervical sympathetic, with early pathological changes and characteristic changes in the vagus. Marie mentions the occurrence of slight exophthalmos.

Nerves.—An important feature of the disease is enlargement of the peripheral nerves. Clinically those most frequently enlarged are the internal cutaneous of the forearm, the ulnar, the saphenous and the superficial cervical nerves. They are increased in volume and are often hard on palpation and may actually be visible under the skin. On the other hand hypertrophy of the accessible nerves may be inconspicuous and may be observed only if sought for or at autopsy.

In this connection it must be remembered that peripheral nerves may be visible or palpable in other conditions and in apparently normal individuals. In a diabetic, aged 58, seen recently, the knee-jerks were sluggish, the ankle-jerks absent and the plantar responses flexor. The left internal saphenous nerve was hard and easily palpable just above the ankle joint. Again, a boy of 19 admitted to hospital with symptoms of gastritis had very sluggish knee- and ankle-jerks, a flexor plantar response and a minor degree of flat foot. Both internal saphenous nerves were easily visible and palpable above the ankle but there were no other signs or symptoms to suggest any nervous disease.

PATHOLOGY.

The pathological changes which occur are fully described and discussed by de Bruyn and Stern and the following is a brief summary of their findings.

The changes are mainly incident upon the peripheral nerves and spinal ganglia. In the former both the interstitial and neural elements are hypertrophied and in the distal portions of the nerves there is much loss of myelin. The characteristic features of the disease-process in the nerves is the presence of masses of tissue, either nucleated or non-nucleated, arising from the sheath of Schwann and constituting hypertrophy of this sheath.

Other authors have described these masses as 'onion bulbs' from their laminated appearance, resembling the cut section of an onion. This lamination was absent from de Bruyn and Stern's case and they suggest that they had observed a different stage in the same morbid process. Similar masses may be present in the spinal ganglia. Marie and Bertrand detected many signs of degeneration in the ganglion-cells and this has been confirmed by de Bruyn and Stern. Degeneration in the posterior columns of the spinal cord has been described in the majority of cases and is considered to be a sequel to the pathological process in the nerves. Some authors have described atrophy of the cells of the anterior horn (Souques and Bertrand, Yokomori, Dejerine and Thomas).

DIAGNOSIS.

The conditions which progressive hypertrophic polyneuritis most resembles are hereditary ataxia (Friedreich's disease), and peroneal muscular atrophy of the Charcot-Marie-Tooth type.

Friedreich's disease is characterised by the absence of tendon-jerks; an extensor plantar response; deformities, pes cavus and scoliosis being the most common; cerebellar signs including ataxia, nystagmus and speech defects. Muscular wasting is not as a rule present, but in a few instances symmetrical wasting of the foot muscles and intrinsic muscles of the hands has been reported. Such cases may be confused with peroneal muscular atrophy or may have been unrecognised cases of progressive hypertrophic neuritis, which itself closely resembles peroneal muscular atrophy. In the latter disease, however, the knee-jerks may be retained, there is no extensor plantar response, kyphoscoliosis does not occur, nor are sensory changes marked. There are no pupillary changes, incoordination of movement or nystagmus. The enlargement of nerves with typical histological changes is peculiar to hypertrophic interstitial neuritis and it is stated that the electrical reactions show more marked changes than in peroneal muscular atrophy.

Hoffmann, Raymond and other writers have affirmed that these conditions are clinical varieties of the same malady; Dejerine and Marie, however, oppose this view.

Symonds and Shaw observed claw-feet with absent tendon-jerks occurring in seven individuals in one family. The main features of their cases were bilateral pes cavus and, in three, wasting of the hand muscles. The tendon-reflexes were absent and the plantar responses, when obtained, flexor. There were no sensory changes. The condition of the peripheral nerves is not mentioned. These writers also refer to seven members of a family with acquired pes cavus and total abolition of the tendon-jerks and, in several, atrophic weakness of the hand muscles, recorded by Roussy and Levy, who regarded their cases as distinct from Friedreich's disease on the one hand and peroneal muscular atrophy on the other. Symonds and Shaw, however, regard both series as a forme fruste of Charcot-Marie-Tooth's disease.

It is evident that progressive hypertrophic polyneuritis bears a close clinical resemblance to some examples of peroneal muscular atrophy; but it must be admitted that the true relationship between them and other similar diseases is at present unknown, and any attempt to classify them is speculative.

It is well known that in any hereditary condition varieties occur which appear to be peculiar to a family and do not accord with the classical descriptions of the malady.

Until further pathological evidence is available to prove their etiological connection, progressive hypertrophic polyneuritis stands out as a sufficiently definite clinical entity to merit description as a separate disease.

COURSE AND PROGNOSIS.

The disease as a rule is a very chronic one, especially in those cases which start in childhood. The deformities, muscular atrophy and enlargement of the nerves are slowly progressive and the associated weakness may ultimately render the patients helpless. Many live to an advanced age. The patients in seven cases collected from the literature were over the age of 50 years, the eldest 74. In de Bruyn and Stern's case, however, death ensued three years after the onset of the condition. Generally there is no shortening of life.

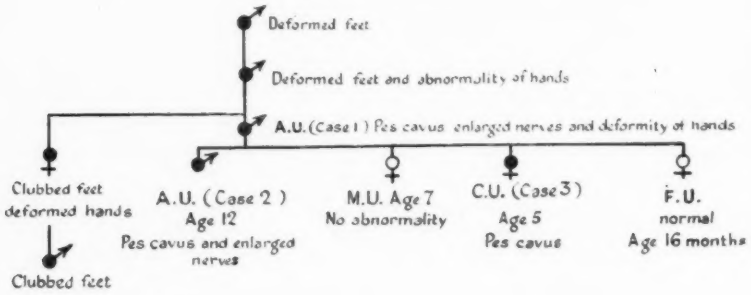
TREATMENT.

A number of cases have received orthopædic treatment for pes cavus in childhood but it is doubtful if any benefit accrued. The progressive nature of the malady renders the prospects for orthopædic surgery unfavourable. The differential diagnosis between this condition and simple deformities therefore becomes of importance to the surgeon.

In the cases of the present series walking is quite satisfactory and all that is required is special boots to fit the deformed feet.

No treatment is known which influences the progress of the disease.

PERSONAL CASES.


Deformed feet
Deformed feet and abnormality of hands
A.U. (Case 1) Pes cavus enlarged nerves and deformity of hands
Clubbed feet deformed hands
A.U. (Case 2) Age 12 Pes cavus and enlarged nerves
M.U. Age 7 No abnormality
C.U. (Case 3) Age 5 Pes cavus
F.U. normal Age 16 months
Clubbed feet

Case 1. A. U., male, age 50.

He states that his father had clubbed feet and also some deformity of the hands. His grandfather had some abnormality of the feet. One elder sister has had clubbed feet all her life, and deformity of the hands. She has a son aged 21 who has a tendency to clubbed feet. His other brothers and sisters are normal.

History.—He first noticed trouble with the feet at the age of nine or ten years. Wasting of the hand muscles has been present for many years but this has caused him no inconvenience until recently, when the wasting has become more marked. He complains specially of weakness of the thumb muscles. Occasional sharp pains in various parts of the body have occurred and sweating of the hands is excessive.

Examination. Muscular system.—There is general muscular maldevelopment. Some kyphoscoliosis is present in the dorsal region, with convexity to the right, and slight lordosis in the lumbar region. There is no focal wasting of the arm muscles. Wasting is present in the muscles of the thenar and hypothenar eminences and interossei of both hands. Fibrillary twitchings are occasionally seen in the triceps and latissimus dorsi.

There is marked weakness of opposition of the thumb and little finger and also of adduction of the thumb. A lesser degree of weakness is also present in dorsiflexion of the wrists.

In the lower limbs the musculature is of subnormal development. Fibrillary twitchings have been seen in the calf muscles from time to time. Pes cavus is present in both feet and is more marked on the right side (fig. 1). The great toe is hyperextended at the metatarsophalangeal joint and acutely flexed at the interphalangeal joint.

FIG. 1.—Case I.

Central nervous system.—Cranial nerves normal. Optic discs normal. No nystagmus. Speech is rather slow but no definite abnormality is present.

Reflexes.—The abdominal reflexes are absent. All tendon-jerks are very sluggish indeed. The right knee-jerk is absent and there is only a flicker of the quadriceps on the left side. Both plantar responses are absent.

Sensory system.—There is slight blunting of sensation to touch, pin-prick, heat and cold. Possibly slight diminution of vibration sense in the left leg. Large and small joint sense is normal. Some incoordination noticed on sliding the heel down the opposite shin, which is more marked in the right leg. Romberg's sign negative. No definite intention-

tremor, but there is some incoordination of the hands on attempting to pick up a pin. The gait is somewhat clumsy and tends to be on rather a wider base than normal, probably due to the deformity of the feet.

Cutaneous nerves.—There is visible enlargement of the internal cutaneous nerve of the right forearm and of the internal saphenous nerves of both feet, most marked just above the ankle joints (fig. 2). The right ulnar nerve is unduly palpable and is enlarged.

FIG. 2.—Case I. The internal saphenous nerve is visible above the right internal malleolus.

Electrical reactions.—The arm and leg muscles respond to faradism and galvanism, but a much stronger current than normal is required to evoke any response.

CASE 2. A. U., male, aged 12.

Pes cavus was first noticed at the age of two to three years but he has not complained until recently when he found that ordinary boots and shoes gave some discomfort to the feet.

Examination.—He walks well and there is no ataxia. Bilateral pes cavus is present and some general muscular atrophy of the legs (fig. 3). There is no sensory loss other

than slight defect of postural sensibility of the toes. All tendon-jerks are very sluggish and both ankle-jerks are absent. The plantar responses are both extensor. The abdominal reflexes are brisk. There is no tremor, Romberg's sign is negative and the finger-nose test is satisfactory. Cranial nerves normal. Optic discs normal. There is no deformity of the back. Electrical reactions normal. There is thickening of the external saphenous nerve on the left side, above the ankle joint.

Fig. 3.—Case II.

Case 3. C. U., female, aged 5.

No previous history of importance. The parents have noticed no abnormality. Well nourished. Slight webbing of the second and third toes of each foot. No definite club foot is present but there is a high arch on each side. Cranial nerves normal. No nystagmus. Optic discs normal. Walking is on rather a wide base but no ataxia has been noticed. Romberg's sign negative. No muscular wasting. The arm-jerks are very sluggish and the right knee- and ankle-jerks are absent. The right plantar response is equivocal. Abdominal reflexes brisk. There is no visible or palpable hypertrophy of nerves.

M. U., female, aged 7, and F. U., female, aged 16 months, the other two children, are both entirely unaffected and no abnormal physical signs were detected.

Cases 1 and 2 were shown at the Neurological Section of the Royal Society of Medicine and are recorded in the *Proceedings* of the Section.

BIOPSY.

A portion of the right internal cutaneous nerve (Case 1) was removed from the forearm, under local anæsthesia. By kind permission of Dr. J. Godwin Greenfield a microscopic examination of the nerve removed was carried out in the laboratory of the National Hospital, Queen Square. The report received is as follows. The piece of nerve resected, about 2″ in length, was rather thicker than a normal internal cutaneous nerve. After fixation in formolsaline, longitudinal and transverse frozen and celloidin sections were made.

In frozen sections stained with Scharlach R and counterstained with hæmatoxylin, the nerve-fibres appeared to be widely separated. The perineurium was greatly thickened, while the endoneurium was so much thickened that each endoneural sheath appeared as a wide concentric ring enclosing the myelin sheath. Occasionally two myelin sheaths were contained within one such endoneural sheath. No lamellar arrangement of the endoneurium was observed. The myelin sheaths were present, and took the stain of normal myelin, but in some parts of the section the thickened endoneurium enclosed clear spaces devoid of myelin. Between the endoneural sheaths there were small areas of a structureless, unstained tissue which contributed to the wide spacing of the nerve-fibres.

In celloidin sections stained with hæmatoxylin and counterstained with Van Gieson's stain there was considerable shrinkage of the tissues inevitable in the process of preparation. In spite of this, wide separation of the nerve-fibres was still evident, and the thickening of the peri- and endoneurium was striking. The nuclei of the endoneurium were seen to be greatly increased in number. The indeterminate tissue between the nerve-fibres stained a faint yellow with this stain. It contained no nuclei. Sections stained by the Weigert Pal method and counterstained with Van Gieson's stain showed that the majority of the nerve-fibres were well myelinated.

In these sections the wide separation of the nerve-fibres was more evident than in the other celloidin sections, as the preliminary mordanting with chrome salts had reduced shrinkage to a minimum. In some areas of the sections thickened endoneural sheaths enclosed myelin sheaths which were thinner than the normal myelin sheaths of sensory fibres.

By Kernohan's modification of Bielschowsky's method the majority of the axis-cylinders appeared normal.

The histological features of this nerve are typical of hypertrophic interstitial neuritis; they conform almost exactly to those described in the biopsy on Russell and Garland's second case. This similarity of the histopathological picture suggests that the disease process has reached approximately the same point in the two cases.

I am greatly indebted to Dr. R. O. Stern for kindly undertaking the histological work and for preparing and reporting on the sections.

My thanks are also due to Dr. Macdonald Critchley for his advice and to Dr. Alan Randle, Medical Superintendent, Mile End Hospital, for his permission to publish the cases.

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THE 'PATH' THEORY OF CORTICAL FUNCTION.*

By

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There have been few general theories to account for the functioning of the central nervous system, but there has been one which, although it has never been put forward with any definite evidence, nevertheless has gradually grown until it remains practically the only theory in the field. I refer to the 'path' theory, which states, roughly, that the functions of the central nervous system are controlled by chains of neurons laid down as a path so as to conduct the impulse to its appropriate end-organ: that the paths are strictly constant, thus accounting for the fact that the reflexes and reactions are largely constant: that learning consists of the opening up of new paths: and that memory consists of the retraversing of some old path by another impulse.

But it is beginning to become apparent that the theory is in need of a thorough overhaul, especially as it has never been clearly stated but tends to lie in the background, emerging to explain some convenient fact yet not being questioned when facts appear which it is powerless to explain. It appears either explicitly or implicitly in neurology, in physiology, and particularly in any work which attempts to deal with physiological psychology: and, curiously enough, it is particularly in the latter that it breaks down. It will be shown that there are certain facts which are incompatible with this theory: but first it is as well to examine its beginnings and its development[1] since this throws some light on its present position.

Galen, about A.D. 190, first showed that an excised muscle may be made to twitch by pinching the nerve. He found that pinching the nerve at any point of its course resulted in contraction, and that division of the nerve between the point of application of the stimulus and the muscle prevented contraction. Here, then, was the first 'path' theory, a theory which was obviously justified by the facts. It was assumed that something passed from the point of stimulation to the muscle and it was found that, given the state of the path, one could predict whether or not the muscle would contract.

From this point there was a gap, but by 1800 the grosser anatomy of the nervous system was well known, though practically nothing was known of its physiology. In 1811, Bell[2] made his fundamental discovery of the functions

* Submitted for publication January, 1931. Since this article was handed to the Editor, Professor K. S. Lashley has, in lectures given at King's College, London, developed a theory similar to that described here. This paper was completed before their delivery.—W. R. A.

of the anterior and posterior spinal roots. It was found that in any reflex the impulse always went in at the posterior roots and always emerged from the anterior roots to go to the muscles. Further it was found that a break in any part of this circuit always abolished the reflex. At this time nothing was known of the histology of the spinal cord and it was naturally imagined that the course of the impulse across the spinal cord was determined by a direct pathway through the cord in the same way as it was determined by the peripheral nerves. These early workers, in fact, imagined that the afferent and efferent nerves were merely two halves of one nerve which ran direct from the skin through the spinal cord to the muscle. Thus in 1822 Bell[3] developed his idea of a ' nervous circle,' and in 1850 Marshall Hall[4] first used the term ' reflex arc.'

At about this time, the microscope was first being used, and the histology of the central nervous system was being investigated. The discovery of the multicellular nature of the spinal cord at first disturbed these ideas, but the postulate of a ' fixed path ' was already well established from the work done on peripheral nerves ; and a chain of nerve-cells was soon postulated in place of the old concept of one continuous nerve from skin to muscle. Since the peripheral path was fixed, it was quite naturally assumed that the path through the spinal cord would also be fixed and immutable. But the theory of a fixed path was postulated, not because the evidence showed that it must be fixed but merely because it was impossible to construct any reasonable theory which allowed the path to vary. It must be remembered that at that time practically the only thing known about nerves was that they conducted impulses. The simple theory that the reflex was controlled and produced by a predetermined path without branches which led straight from skin to muscle through the spinal cord was easy to understand and fitted the few facts quite well.

Lewes[5] in 1867 was among the first to criticise this theory, and his criticism holds good to-day. He attacked the evidence for the existence of the anatomical structures which are assumed to underlie reflex action. He pointed out that it is a case of ' an imaginary physiology based on an imaginary anatomy.' To quote his words :—" The sensory nerve is not seen to enter the spinal cord and to pass over along a particular path to a corresponding point of exit. It is seen to enter the gray substance, which is continuous throughout the spinal cord ; *it is there lost to view, its course being untraceable* " (my italics). He concludes that it is the physiology of the central nervous system which controls the reflexes, and not its macroscopic or microscopic anatomy.

Since then, the neurologists in particular have been mapping out tract after tract in the nervous system, until the conclusion seems obviously to be that ' all is tracts.' But there is a tendency to forget that all these tracts are *white matter* tracts and that, as far as is known, no single gray matter tract has ever been discovered. It is not permissible to ignore the essential difference between the gray and the white matter. The two are fundamentally

different, and analogies from the one to the other are not permissible. The gray matter is the essential substance of the central nervous system, and it is in this substance that all the purposive, integrative functions of the nervous system are worked out. But the body and brain are large, and the gray matter is not sufficient to extend all over the body ; so, to connect up the masses of gray matter with one another and with the muscles, glands, etc., a highly specialised connecting tissue is developed—the white matter, a tissue apparently devoid of all functions save that of conduction. The white matter is obviously constructed as a ' path ' system, but this does not entitle us to draw the conclusion that the gray matter will also be built on the same plan, since the functions of the two types are so different.

The ' path ' theory of gray matter function, originated and developed by neurologists in their work on the conduction tracts of the nervous system, has slowly crept in, almost without being noticed. The standard text-book diagram of a spinal reflex, for instance, begs the question at the outset with its picture of afferent and efferent fibres, which are known to be immutable, shown connected together by a single cell, thereby suggesting strongly to all who read that the whole mechanism is known to be that of a path, and that this path could be dissected out if only our technique were good enough. Herrick[6] writes of these diagrams as follows :—" The simplified neurologic schemata which we use as pædagogic devices are necessary instruments for unlocking those doors of the student's mind which lead into the more recondite secrets of nervous organization. But having opened the door in this way, the key should be laid aside and not regarded as even an adequate symbol of the actual organization, as is so often done in both clinical and psychological practice."

The text-book diagram, having ' explained ' the mechanism of reflex action, is succeeded by other diagrams showing how summation, inhibition, etc., may also be explained in terms of paths. From this it is but a short step to the explanation of all nervous activity by means of ' permanent path ' mechanisms. Association is assumed to consist of the linking up of nerve-cells ; memory is explained as the re-threading of an old path by a fresh impulse, and it is added that, of course, the passage of an impulse lowers the resistance of the synapses, and so on. But examples need not be multiplied. Lashley[7] in a recent paper has pointed out that many of the current ' explanations ' have no basis in fact. To take one definite instance—the idea that the passage of an impulse lowers the resistance of a synapse—there is no evidence, clinical or experimental, for this idea, yet it is met with repeatedly.

There is one other ' fact ' which must be mentioned since unless it is refuted it is apt to be used as a proof of the path theory. I refer to the assumption of the constancy of the path of the impulses in a simple reflex. It is usually assumed, almost axiomatically, that the path followed by the impulses in a simple reflex such as the corneal is constant in its passage from neuron to neuron. It must be pointed out that this is not a fact but a hypothesis—a

hypothesis supported, incidentally, by little or no evidence. Whether the impulses take the same path each time or whether they take a variable path must at present be considered an open question.

There is a second fault in the diagram type of explanation. It lies in the supposition that a reaction may be broken down into its individual impulses and that the reaction may be adequately examined by examining the paths of the individual impulses. This, although a common idea, cannot be entertained. Many impulses come up the same nerve-fibre many times a day—consider for instance one of the sensory nerves of the leg. But in each case, what happens to the impulse depends on what other impulses ' say ' about the situation. It is fairly clear that the cerebral cortex reacts to stimuli not as if they were a mass of independent stimuli but as an interconnected and integrated bunch. If one may use an analogy for purposes of illustration, one may compare the original individual impulses to the pieces of a jig-saw puzzle. The cortex does not merely react to each piece of the puzzle, it assembles them into a connected picture, which is obviously something quite different from the arithmetical sum of the individual pieces. Having assembled the picture, the brain then reacts to the picture as a whole. This, of course, is really only pointing out anew that the function of the brain is integrative, and not merely summative. The methods of explanation which deal with isolated stimuli are therefore fallacious.

After these preliminary remarks we may pass to the actual clinical and experimental evidence which is against the path theory of cortical function.

The extent to which the nervous system is independent of localized injuries has been strikingly demonstrated by Lashley[8,9,10], who has been working on the maze-habit in rats, and its relation to cortical injury. He took a number of rats and taught them a given maze. He then operated on them and destroyed various parts of the cortex, removing different parts in different rats, so that altogether he had removed any given part of the cortex in at least one rat. When they had recovered he put them in the maze again, to see how much they had altered. He found that any part of the cortex could learn the maze-habit, and that no part of the cortex showed any superiority over any other part. Frontal, visual, parietal cortices, all were just as capable of learning the maze-habit as any other part. On testing them in mazes of varying difficulty, he found that the rat's ability to learn a difficult maze depended solely on the amount of cortex left behind, again not depending in the least on the position of the cortex left.

From this and from the rest of his work he[8,9] has developed the concept of the ' equipotentiality of the cortex,' meaning by that that all parts are equivalent for learning, that the cortex acts as a whole in any given reaction, and that its ability depends almost entirely on the amount of cortex available. The position of the lesion appears to be without significance. " The cortex, after an injury, promptly readjusts itself, but in virtue of its lowered mass,

at a lower level." He ends with the following conclusion :—" Such phenomena suggest that the nervous system is capable of a self-regulation which gives a coherent logical character to its functioning no matter how its anatomical constituents may be disturbed." Such a conclusion is clearly against the rigorously anatomical path theory.

These results are very similar to those obtained by Pavlov[11] in his attempts to localise the conditioned reflex in the cortex. He took many dogs, established a conditioned reflex in them and then tried to destroy the reflex by incisions through the cortex. These incisions should, on the path theory, cut through the path if the cuts were sufficiently numerous. He found, like Lashley, that the conditioned reflex seemed to have no definite localisation in the cortex, although he had previously shown conclusively that the conditioned reflex depends upon, and uses, the cerebral cortex.

Such results as these are clearly against the path theory. The cortex evidently does not consist of a number of fixed paths, one to each reaction.

Similar evidence against the theory is furnished by observation of brain injuries in man, such as by tumour, etc. Injury to the cortex will obviously destroy certain nerve-cells and their connections. On the path theory we should expect that the patient would lose those reactions which depended on the paths which have been cut, and would retain all others. In practice, this sharp-cut loss of reactions is not seen in the majority of cases. The patient, for instance, does not forget his name while remembering his address : nor does he remember his aunt's name while forgetting that of his dog. On the contrary, the disturbance shown seems to be like that observed by Lashley in rats, viz., that there is a general lowering of intelligence, so that all simple things tend to be remembered while all complicated matters tend to be forgotten. This state is quite different from the condition to be expected from the path theory, where we would have expected a complete loss of a number of specific reactions, side by side with complete normality in other reactions, the result in any given reaction depending on whether the path for the reaction was cut or not.

Of a different type but of similar import are the experiments of Marina[12]. He crossed the internal and external recti muscles of the eye on one side in apes and found that, as soon as the wounds were healed, the eyes moved normally and together. According to the path theory, inversely conjugate movements should have ensued since the paths were crossed. If it is objected that the nerve centres almost instantly recrossed the paths, one may justly ask why should a path once firmly laid down ever bother to recross itself ? The path theory suggests that the eyes would probably go on moving contrariwise indefinitely, for it offers no reason as to why the paths should ever be altered once they are laid down, especially since the continuous passage of impulses should have worn the path into a deep rut. From this and from many other similar experiments Marina concluded that the conduction pathways have no predestined function. He demanded a new foundation for the physiology of the brain.

There is yet a third type of experiment which shows how impotent the path theory is to account for the facts.

To explain the phenomenon of the subsequent recognition of objects once seen, the obvious explanation according to the path theory is that the object, by stimulating a particular group of cells in the retina, thereby stimulates a particular group of cells in the visual cortex. Should this group be stimulated again in the same way, the similar excitation resulting is ' recognised ' by the cortex as being the same as previously and the object itself is thereby recognised.

But this idea, however simple it may appear at first, soon breaks down when one considers the various ways in which the object may vary its projection on the retina without the faculty of recognition being upset. For instance, I may see an object in one part of the visual field and note its appearance. Later I may catch sight of the same object in another part of the visual field altogether, but I recognise it at once, and without any difficulty, in spite of the fact that the object is now stimulating a group of cells, *not one of which was necessarily concerned in the original seeing*. It is obvious that the path theory breaks down under these circumstances. There is, in fact, no end to the transformations which an object may undergo without affecting the ability to recognise it. These transformations (of position) all have the effect of stimulating quite a different group of nerve-cells in the retina and visual cortex, without having any effect on the ability to recognise the object. Thus the object may first be placed vertically; it is then placed on its side and re-inspected—it is recognised at once. It may be brought nearer the eye, thus increasing the area over which it stimulates the retina. It may be moved away until it is near the limit of definition. It may be reversed by viewing it in a mirror so that its mirror-image is seen. All day long in everyday life we are continuously recognising things that we have never before seen in exactly that position. In all these transformations, the object in its second position may stimulate a group of cells in the retina and visual cortex quite different from those stimulated on the first viewing, yet the object is recognised at once.

From these results we can see that the recognition of an object is independent of the cells it stimulates. It is the pattern which counts, not the position.

What, then, are we to substitute for the path theory ?

I propose here to sketch out a possible alternative theory, not so much to suggest that it is definitely the actual state of affairs in the nervous system, but chiefly in order to demonstrate practically that there are alternative theories, since there seems to be a general impression that there is no alternative theory —that the nervous system must, a priori, work on a ' path ' mechanism. On the contrary, the path theory has no such a priori validity. That there is at least one alternative theory will be shown below.

Let us consider first the question of the equivalence of the different images thrown on the visual cortex by a given object. We saw above that it is the

pattern that counts, not the position of the pattern. We have to ask what type of mechanism would produce this result.

A mechanism of this type exists in nature. Consider a pond being affected by ripples. We may suppose the pond to have in it a rod which taps the water at certain intervals. Around the rod would develop a system of ripples, forming a definite pattern. If the rod continued to tap the water in the same way, then the pattern formed would remain constant as long as the tapping continued. In the simple case of a single rod it would, of course, form a series of concentric circles. Now stop the tapping, allow the water to settle down, and then recommence the same tapping at another part of the pond—the same system of wave-patterns will again be formed. Here, then, we have a mechanism which shows the features desired ; we have a permanent pattern which is independent of the localisation of the pattern. The wave-system may be more complex without in the least altering the fundamental features. The tapping may be done by a number of rods, all going at different speeds. In this case, of course, the pattern produced will be complex and will exhibit not merely waves but also interference phenomena, but nevertheless, if the same set of rods beating in the same way be started in another part of the pond, then the pattern will develop in just the same way again. This pattern is quite independent of its localisation in the pond, and its nature will depend solely on the number, position and frequency of the stimuli (rods) producing it. It may, however, be affected by the water in certain ways. Firstly, if the water is at all ' patchy ' in its nature, say in temperature, then the pattern will not work itself out in the same way in different places, but the pattern produced will depend upon the distribution of temperatures in the two areas. Further, if the water be changed uniformly, say by being changed to treacle, then the pattern will change, but in this case it will merely suffer a uniform change by becoming smaller.

The case of ripples on water has been considered because it is simple and well-known. Actually there are many such systems known, all of which show the same fundamental properties, viz., that there is a fixed pattern movable over a material substratum in such a way that the form of the pattern is independent of the position of the pattern. In all such cases, the nature of the pattern developed depends upon (*a*) the timing, nature, etc., of the rods producing it, and (*b*) on the functional, physiological or dynamic laws regulating the behaviour of the substratum.

It is suggested that in the central nervous system the stimuli enter and work themselves out as a pattern of nerve impulses on the cortex or gray matter generally, and that they are dependent on the cortex only in so far as the cortex provides a suitable medium on which the pattern can move and develop. According to such a hypothesis, a visual pattern thrown on to the visual cortex would not lie there as a static, fixed pattern, nor would it be projected *en bloc* to some other part of the cortex, but it would immediately

grow, spread and irradiate over the whole cortex, just like the ripples spreading over the pond. Now there is in this connexion a well-established experimental fact, which shows that stimuli do in fact tend to spread over the cortex in this manner. I refer to the phenomenon of ' irradiation ' described by Pavlov[11]. He has shown that any stimulus which arrives at the cortex immediately begins to spread over the surrounding cortex. He[13] is of the opinion that this phenomenon is of fundamental importance in the physiology of the cerebral cortex. Now according to the path theory, this phenomenon has no meaning whatsoever. In fact, such an occurrence in a system run on path lines would lead immediately to chaos. The path theory and the fact of ' irradiation ' are, as far as one can see, mutually exclusive and contradictory. On the other hand, the phenomenon of irradiation and what we may call the ' pattern ' or ' ripple ' theory of cortical function, are mutually complementary. The ' pattern ' theory needs irradiation in order that the pattern may develop, while if one is given irradiation, then one may draw the logical conclusion that if one impulse spreads, a group of impulses will also spread, and of course the result of the spreading will depend on the distribution of stimuli in the original pattern and on the nature of the medium over which it spreads.

Such a theory would fit the facts of the recognition of objects in different parts of the visual field. For just like the ripples in the pond of water, so would the pattern developed depend solely on the rhythm and distribution of the stimuli, and not at all on the place stimulated.

Lashley[7,8] has pointed out in this connexion that wherever the distribution of the stimuli in space is of importance, one will find a spatial projection of the fibres on the cortex. It is, of course, in vision above all where the distribution of the stimuli in space is of importance, and in the visual cortex we find an accurate projection of the retina. To take the opposite extreme, although high and low notes are recognised in music, yet this has no distinction in space and correspondingly we find no scalar projection of musical notes on the cortex. Lashley has pointed out that this fact has no meaning in the path theory. On the other hand, for the pattern theory it is of fundamental importance that it should be so, for the impulses or ' ripples ' must be given a correct start if they are going to irradiate and spread to form a correct pattern.

The pattern theory would also clarify to some extent the present confusion regarding the exact position of the ' functional ' disorders of the nervous system. To return to the analogy of the pond and its ripples for a moment, we see that there are two separate and distinct ways in which an abnormal or unusual pattern may be produced. Firstly by changes in the underlying medium on which the ripples form—there might be a rock in the water, or the water might be patchy in temperature, or the whole water might change in viscosity, or there might be a log floating on the surface. All these abnormalities would be disturbances of the underlying medium and as such would naturally affect adversely any pattern developing on its surface. Such abnormalities would

correspond to the abnormalities of behaviour produced in the living organism by such things as tumours, infections, toxins, etc. It may be noted that such an obstruction would interfere not with any given pattern (or reaction) but would tend to interfere most with the most complex patterns, and this, it is suggested, is similar to what is observed in organic cortical disturbances.

But there is a second type of disturbance which may be produced, viz., by abnormalities of the original stimuli which produce the pattern. Here the underlying medium, the water or the cortex, is perfectly normal, but it has abnormal or unusual stimuli thrown on it. The result, naturally, will be an abnormal pattern, but produced, not by any abnormality of the water (or cortex), but by the fact that the stimuli which started the pattern were abnormal. This, I would suggest, is a state of affairs comparable to the 'functional' disorders. There are thus two fundamental ways in which such a system may go wrong: firstly because of an abnormality in the underlying medium, and secondly because of an abnormality in the stimuli producing the pattern. At this point I wish to introduce a proposition which would require separate consideration for its complete exposition. It is to the effect that the concept of 'psychogenesis' is equivalent to stating that the cause of abnormalities of behaviour lies in the fact that the individual is subjected to abnormal or unusual stimuli which are too conflicting with his previous experience to enable him to react adequately. Most psychogenesists are agreed, I believe, that the cause of abnormalities of behaviour lies in the environment; the latter can only influence the individual as stimuli. That this type of disorder exists has been shown clearly by Pavlov[11]. He has produced severe 'functional' breakdowns in dogs by subjecting them to stimuli which were neither frightening, nor loud, nor dazzling nor in any way harmful, but which were violently pathogenic simply because they were selected to conflict strongly with previously established reflexes. Abnormalities of behaviour, therefore, may be produced both by abnormalities of the brain and by abnormalities of the stimuli to which it is subjected.

It will be obvious that, according to the pattern theory, not only is there no conflict between the physiogenic and psychogenic theories of abnormalities of behaviour, but that, on the contrary, two such branches of knowledge are necessary: one to explain what will happen if the underlying medium is abnormal, and the other to explain what will happen if unusual groups of stimuli are presented.

It is interesting to note that in the second type of disorder, due to abnormal stimuli, the cortex will receive the impulses and will then use its own, perfectly normal methods for dealing with them, just as, in the pond, the water will deal perfectly normally with any pattern thrown upon it. Wilson[14] has pointed out that from the neurological aspect the hysteric uses normal mechanisms for the development of his symptoms, while the psychologists, especially the psychoanalysts, have equally recognised that in investigating the mechanisms

of psychopathology they find nothing but normal physiological mechanisms, acting on abnormal environmental material.

The pattern theory has been elaborated chiefly from the facts of cortical function, but we may justly enquire whether it has anything to say about reflex action. In its outline the theory has little to say except this—that since it is practically certain that the mechanisms of the brain and spinal cord will turn out to be essentially the same, we must therefore draw the conclusion that if the path theory will not fit cortical function, then it must be rejected as an explanation of reflex function. It was for this reason that I pointed out above that there is no evidence for the assumed constancy of the path of impulses in reflex action. Bourguignon's[15] work on chronaxy strongly suggests, in fact, that the afferent impulses in the reflexes also irradiate diffusely in the gray matter but they can only escape from the spinal cord and show themselves down that nerve which has the same chronaxy. We may therefore, I think, invert the usual proceeding, and draw from the cortex conclusions regarding the mechanisms of reflex action.

Any value which the theory proposed may possess lies not in the immediate results achieved, but in the fact that it clears the ground, that it supplies an alternative to the path theory, and that it provides a new orientation to the subject, for a new orientation to the subject is certainly needed.

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Editorial.

EXTRAPYRAMIDAL CENTRAL MECHANISMS.

TWO well-known physiological observations conspired to direct thought towards a particular theory of nervous control of animal action. These two observations were the specific and restricted nature of most spinal reflexes evoked by moderate stimuli; and the similar specific and restricted nature of the motor responses to stimulation of points in the excitable area of the frontal lobe of the cerebrum—again when the stimuli are of not too great intensity. When attention was directed to the natural behaviour of normal animals it was easy to speculate that the total activity was a compound of unit activities. Where such compound reactions occur after lesions which have eliminated the motor action of the cerebral cortex (as in the decerebrate animal or in animals deprived of portions of the motor cortex alone) the combined activity might well be supposed to be a compound made up of individual reflexes and co-ordinated by subcortical mechanisms. Where however the combined activity was obviously directed to an external object through one or more of the higher organs of sense, the compound activity might be regarded as brought about by a multiple excitement of the motor mechanisms in the cerebral cortex. In this latter case, the action of the whole animal might be looked upon as compounded of a large number of individual cortical motor actions—as if the motor cortex was being artificially stimulated at a multitude of different points. Such a manner of regarding the complex reactions of an animal to auditory and visual stimuli is certainly a plausible one, and it is possible that this view of cortical activity is held (with reservavations) by the majority of workers who interest themselves in this field.

During an interesting discussion at the Neurological Congress in Berne this summer, attention was again drawn to the curious motor reaction which may be obtained on faradic stimulation of the exposed cut surface of the mid-brain at or near the locus of the red nucleus. The reactions in question are reactions of the whole animal, and to that extent differ com-

pletely from the reactions obtainable on stimulation of the adjacent crus cerebri—for these latter reactions are confined to the opposite side of the body. From this area (and we may add in parentheses, from higher parts of the central nervous system) a combined reaction may be evoked and is certainly not brought about by the simultaneous stimulation of a multitude of different nerve fibres in the corticospinal tract. Further, Ranson's careful reinvestigation of these phenomena in cats has confirmed the original observations in monkeys that a curious antagonism appears to exist between them and the reactions elicited from the corticospinal tract itself. The stimulation of the area in question elicits (amongst other things) a long-maintained flexion of the same-sided fore-limb. Similar stimulation of the crossed crus cerebri also elicits flexion of that individual limb. If now the first area be stimulated and the stimulation be stopped, a long-continued flexion of the limb persists. If, during this, the crus be stimulated, the flexion may be augmented slightly. But on cessation of stimulation the arm ' flops.' The corticospinal activity, although in the same sense as this other activity, differs in this, that it appears to wipe out the long-continued after-discharge which would otherwise follow the first stimulation. In other words, the cortical reaction appears to leave behind it a clean slate. It is interesting, but not germane to our present argument, that Ranson's confirmation and expansion of previous observations on the effect of lesions upon the reaction obtained from the ' red nuclear area ' have led him to the opinion that the reaction cannot be subserved by any of the well-established descending motor tracts.

Work which has been reported on, but is at present unpublished, indicates that somewhat similar reactions of the whole animal follow stimulation of higher parts of the central nervous system—for instance, in the region of the optic thalamus, and elsewhere. These reactions differ from what may be termed the ' red nuclear reaction ' in various respects ; one particular being, for instance, that phasic movements of one or more limbs may occur. In some cases the fore-limb may exhibit definite slashing or scratching movements. In other cases it may merely be poised as if about to strike, and with claws protruded (in the case of the cat). In all cases these reactions correspond to the ' red nuclear reaction ' in being brought about by extrapyramidal mechanisms ; in all cases they differ from normal cortical activities in being undirected to any external object.

Such results seem to point to a different conception of the mechanism by which the total activity of an animal is brought about. In place of the old idea that these activities are a concatenation of individual cortical reactions, it would appear more likely that they are governed by some quite different nervous mechanism. The opinion may be hazarded that a subcortical mechanism acts, in a sense independently, in bringing about total activities of a more or less general nature ; and that the cortical mechanism functions by producing the small variations necessary to direct such actions to a particular object. But to say this is certainly to err too much on the other side, and to underestimate the functions of the cortex to which, for instance, the phenomena here described would seem to add the power of inhibiting the subcortical mechanism and allowing it or a similar one to function in another direction.

Abstracts.

Neurology.

NEURO-ANATOMY AND NEUROPHYSIOLOGY.

[38] **The elastic layer in the cerebral vessels: studies of the newborn and of children.**—C. R. Tuthill. *Arch. of Neurol. and Psychiat.*, 1931, xxvi, 268.

In a study of the cerebral vessels of two stillborn fœtuses and of twenty-four children, varying in age from birth to 14 years, it was observed for the first time that the size of the vessel determines the presence and the thickness of the elastic layer at birth and also the period of its most active growth. For the large vessels this period is the first three months, whereas for the smaller ones it is for the first five years, although the elastic layer continues to grow throughout childhood.

Splitting of the elastic layer into knotty areas of elastic fibres or lamellæ and long slender cells is present at birth: it is found near the branching of the vessel. Three types of splitting were observed, varying in frequency and in type according to the individual rather than to age.

Retrogressive changes occur in these areas even in childhood, as calcification was found in the split elastic fibres in a child of seven years with an occipital abscess of four months' duration. In six cases, raised areas of split elastic fibres, connective tissue and long slender cells were observed for long distances in the intima without apparent relation to the branching of the vessel. However, the similarity of these six areas to the split elastic fibres before and at the branching of the vessel indicates that they represent a similar process of growth but that, probably owing to the influence of intoxication and inflammation, the splitting of the elastic layer has increased. R. M. S.

[39] **The contralateral flexor reflex, rebound phenomena, co-contraction and reciprocal innervation in spinal and in decerebrate cats.**—S.W. Ranson and J. C. Hinsey. *Arch. of Neurol. and Psychiat.*, 1931, xxvi, 247.

The authors studied the reflexes at the ankle joint in response to electrical stimulation of sensory nerves of the same or of the opposite limb. Spinal, decapitate and decerebrate cats were used.

The response elicited was found to be ipsilateral flexion or extension or contralateral flexion or extension, depending on the neural balance between the spinal reflex centres, the nerve stimulated and the strength of the induction shocks. In chronic spinal cats, with the balance tipped to the flexor side, the usual response to moderately strong stimulation is bilateral flexion.

In decerebrate cats, with the balance tipped toward the extensor side, the usual response is ipsilateral flexion and contralateral extension. Not infrequently the two antagonistic muscles contract simultaneously during the stimulus. Reciprocal innervation can most easily be demonstrated when the extensor muscles are in tonic contraction. Under these conditions any flexor-producing stimulus, whether ipsilateral or contralateral, will cause extensor relaxation. It is maintained that the law of reciprocal innervation cannot properly be interpreted as excluding the possibility of simultaneous contraction. Both simultaneous contraction and reciprocal innervation occur and are essential for the proper functioning of the limbs in standing and walking.

Terminal rebound phenomena—rebound contraction after inhibition, rebound contraction after excitation, rebound relaxation after inhibition and rhythmic rebounds—are described and discussed. The type of reflex response elicited may sometimes be reversed from flexion to extension, or vice versa, by changing the strength or rate of the stimulus or by shifting the electrode from the tibial to the saphenous nerve, by changing the passive posture of the limb and in some other ways.

The significance of these phenomena for an understanding of the organisation of the spinal reflex centres is discussed. R. M. S.

[40] **Studies of the biochemistry of the brain blood by internal jugular puncture.**—Abraham Myerson and Roy D. Halloran. *Amer. Jour. of Psychiat.*, 1930, x, 389.

The introduction of the internal jugular method has made it possible to study the brain metabolism in a direct way, if it is combined, as in this study, with puncture of the carotid artery and, for comparison, with arm blood by a puncture of the brachial artery and basilic vein. This technique is perfectly safe. The specific gravity, sedimentation rate, urea nitrogen, non-protein nitrogen, phosphates, calcium, and chloride content of the blood in the jugular vein, carotid artery, brachial artery, and basilic vein are substantially the same. Sugar disappears in the transit between the carotid artery and the internal jugular vein in much the same way as in the transit between the brachial artery and the basilic vein. Oxygen disappears in the transit between the carotid artery and the internal jugular vein and CO content increases in the same transit. In four cases studied during anæsthetization it was found that the sugar content of the blood rose very decidedly. Before anæsthetization, however, there was a decided difference between the carotid sugar content and jugular sugar content. This difference tended to disappear during anæsthetization. C. S. R.

NEUROPATHOLOGY.

[41] **Affections of the ependyma and their pathogenesis** (Ependimopatie e loro patogenesi).—P. Redaelli. *Riv. di pat. nerv. e ment.*, 1931, xxxvii, 309.

The author has examined 27 cases of atrophic alteration of the walls of the cerebral ventricles in elderly people. These included 15 cases of granular ependymopathy, three of the reticulate variety, and three of the varioliform ependymopathy of Pierre Marie. After having traced in each of them the histopathological picture, he discusses the etiological factors, and lays stress on the extreme complexity and diversity of this in each form. He concerns himself particularly with the granular variety and describes a series of physico-chemical disturbances which specially affect the marginal glia beneath the ependyma. The same marginal glia is concerned in a variety of ways with the genesis of ependymal gliosis and gliomatosis. With regard to the varioliform ependymopathy of Pierre Marie, he considers that it is primarily concerned with the glial elements according to the hypothesis of Nageotte, and does not arise from the degeneration of perivascular adventitia. R. G. G.

[42] **The origin and formation of senile plaques.**—A. Ferraro. *Arch. of Neurol. and Psychiat.*, 1931, xxvi, 1042.

Senile plaques were first described in 1892 by Blocq and Marinesco, who called them sclerotic plaques of neuroglia, a name which was later changed by Redlich to miliary sclerosis. They may originate from both neuroglial elements and from nerve-cells.

Of the neuroglial elements the oligodendroglia cells give origin to some of the plaques, while the astrocytes do not seem to participate in their histogenesis. Conversely, the microglia cells represent an important element from which senile plaques primarily develop. Senile plaques may also originate from isolated disintegrated nerve-cells or from a collection of such elements. The histochemical process that leads to the transformation of a cellular element into a senile plaque is as yet unknown. All that Ferraro can say is that it leads to the formation of a granular argyrophile substance which gives at times, in the central portion of the plaque, some of the reactions of amyloid substance, and at other times the reaction of fat substance. Once the plaque is formed, its development in size and in volume depends on the participation of nerve-cells, microglia, oligodendroglia and, less frequently, astrocytes. Of the cells that do contribute largely to the development of the plaques, the microglia constitutes the largest number. Nerve-cells also participate in the development of the senile plaque through a process of disintegration.

R. M. S.

[43] **The oligodendrogliomas.**—S. T. KWAN and B. J. ALPERS. *Arch. of Neurol. and Psychiat.*, 1931, xxvi, 279.

IN a lavishly illustrated paper the authors give a complete presentation of the histological features of the oligodendroglioma, based on a study of four cases. They confirm the observation that these tumours are composed of oligogliocytes. R. M. S.

[44] **The etiology of disseminated sclerosis** (Sulla etiologia della sclerosi in placche : ricerche sulla cosidetta ' spherula insularis ').—V. TRONCONI. *Boll. Soc. Med.-Chir. di Pavia*, 1931, xlv, 3.

THE author has followed the technique of Chevassut in four cases of disseminated sclerosis, and is unable to confirm the view assigning pathogenic value to the ' spherula insularis.' J. V.

[45] **Reflexes of the carotid sinus in neuropathology** (Les reflexes du sinus carotidien en pathologie nerveuse).—G. MARINESCO and A. KREINDLER. *Jour. de physiol. et de path. gén.*, 1931, xxix, 77.

IN addition to the well-known reflexes of the carotid sinus (cardio-inhibitory, respiratory, and that of arterial tension) the authors have been able to demonstrate another reflex characterised by descent in the plethysmographic curve during compression of the sinuses.

The excitability of the sinuses is diminished in epilepsy and is revealed by reduction of all the reflexes depending on that vascular segment. This hyposensibility explains the instability of vasomotor mechanisms and of arterial tension in the affection. In certain organic nervous diseases of the brain, and in some cases of epilepsy, compression of the sinuses initiates convulsive attacks.

The favourable effect of phenylethylmalonylurea in epilepsy is explained in part by its sensitising action on the carotid sinuses.

In encephalitic Parkinsonism the respiratory reflex of the sinus undergoes modification, and its vasomotor reflex is diminished in myasthenia and uprarenal insufficiency. J. V.

[46] **Human sweat secretion and its relations to the nervous system** (Die Schweisssekretion des Menschen in ihren Beziehungen zum Nervensystem).—L. GUTTMAN. *Zeits. f. d. g. Neurol. u. Psychiat.*, 1931, cxxxv, 1.

THIS is a very long and elaborate study of the clinico-physiological and clinico-pathological aspects of sweat secretion in their relation to the functions and lesions of the nervous system at all levels, from the peripheral to the cortical.

The method used for demonstration is that of Victor Minor, and a full description of the technique is supplied. The details of the various investigations are of considerable clinical interest, and for these, with the tables indicating the spinal segmental supply of the dermatomes from the sudatory standpoint, the original should be consulted.

J. S. P.

[47] **The effect of injections of iodized oil in the spinal subarachnoid space.**—Loyal Davis, H. A. Haven, and T. T. Stone. *Jour. Amer. Med. Assoc.*, 1930, xciv, 772.

It will not surprise some neurologists that the conclusions of the writers, here quoted in extenso, are critical of the value of lipiodol injection.

'1. In twenty-nine of thirty-one cases a definite clinical localisation was possible without the use of iodized oil as a diagnostic aid. We believe, therefore, that in the great majority of cases a definite spinal cord localisation can be made by careful clinical examination.

2. In ten animals injected with iodized oil intracisternally, definite evidences of leptomeningeal reaction, fat encystment and degenerative changes in the gray matter were found. We conclude, therefore, that the injection of iodized oil into the subarachnoid space is to be regarded as a dangerous procedure.'

J. V.

[48] **Further results with the Boltz acetic anhydride test.**—J. Ernest Nicole and E. J. Fitzgerald. *Jour. of Ment. Sci.*, 1931, lxxvii, 321.

The Boltz test is rarely positive in non-paretic cases except in certain conditions of meningeal involvement, such as are but infrequently found in mental hospital work. It is not invariably positive in general paralysis, and a negative Boltz is of little diagnostic value. It agrees with no other usual test, though it probably disagrees less with the Lange than with, say, the globulin reactions. It readily becomes negative after malarial treatment, but mostly so after some years have elapsed since the first attack of malaria. The test does not depend only on the globulin content of the cerebrospinal fluid, or on the total protein increase, or the protein partition, though it probably does bear a relationship to the total tryptophane value of the fluid proteins, and perhaps also to cholesterol. If the test is to be further investigated, it would be preferable to use it in its Hopkins-Cole form, because (*a*) the Hopkins-Cole reagent can be standardized, (*b*) the colour reactions can be graded so as to render it quantitative, and (*c*) there is not the brown charring found when using acetic anhydride.

C. S. R.

SENSORIMOTOR NEUROLOGY.

[49] **Juvenile amaurotic idiocy** (Die juvenile amaurotische Idiotie).—T. SJÖGREN. *Hereditas*, 1931, xiv, 197.

THIS communication amounts in reality to a monograph on the subject with which it deals, and is rich in clinical and genealogical detail. Many family trees are illustrated, and numerous tables bearing on various aspects of the question furnished. Apparently the affection is less rare in Sweden than elsewhere. Some good clinical photographs are reproduced.

Among the author's conclusions the following may be noticed.

1. The ophthalmological changes together with the development and establishment of the neurological syndrome exhibit a remarkable unity and constancy in their progressive course. Attention is directed to the extrapyramidal symptom-complex, the motor disorders, the gait, and the hypertonus. Even when it occurs in an isolated case the syndrome can scarcely be mistaken.

2. In all probability the disease pursues a recessive, monohybrid course from the standpoint of inheritance. Hereditarily and biologically considered, it differs substantially from the infantile variety.

3. There is a curious tendency for the heterozygotic predecessors to congregate in certain restricted regions of the country.

4. In the relatives of the families investigated the occurrence of dementia præcox, oligophrenia, and epilepsy is frequently noted, though whether of higher average than in the country as a whole has not been determined.

J. V.

[50] **Post-vaccinal encephalomyelitis in Holland** (Die in Holland beobachteten Fälle von Encephalomyelitis post-vaccinalis bis zum 1. Jan., 1929).—F. S. BASTIAANSE. *Zeits. f. d. g. Neurol. u. Psychiat.*, 1931, cxxxiv, 657.

DR. BASTIAANSE supplies the reader with an exhaustive and authoritative account of the cases of encephalomyelitis following vaccination which have been observed in Holland and of which 138 are analysed in tabular form. He states that the number has by the end of 1929 exceeded 200, and that at the time of writing 87 cases had occurred in England, 20 in Austria, 21 in France, 26 in Italy, and 85 in Germany.

Of the various conclusions to which the author is led by a careful discussion of his material, clinical and pathological, the following deserve notice.

1. There are so many objections to the view that vaccine virus itself causes the encephalitis that it must be considered in the highest degree improbable.

2. The view assigning the brain disorder to the combined action of another virus and of the vaccine seems supported by many considerations. It is not proved that the former is that of epidemic encephalitis, nor is this likely, for various reasons. Nevertheless it is not proved that the virus cannot be that just mentioned.

3. Possibly a virus as yet altogether unknown and unidentified becomes pathogenic under the influence of the vaccine.

Apparently Dr. Bastiaanse considers it possible that two factors, working simultaneously, are responsible, viz. (1) a latent local infection and (2) a latent infection of the calf through a virus which when combined in a calf vaccine becomes pathogenic for man. The former 'local' infection refers to the existence of some infection latent in a family or in a district, and receives some support from the observed facts (here quoted) of the outbreak of 'influenza' or some condition described as influenza among one or two of a series of cases vaccinated on the same day, while one or two of the same series also subsequently developed the true encephalitis under discussion.

S. A. K. W.

[51] **Nonsuppurative encephalomyelitis accompanying chickenpox.**—H. M. Zimmerman and H. Yannet. *Arch. of Neurol. and Psychiat.*, 1931, xxvi, 322.

The history is presented of a white girl, aged 13 months, who on the third day following the appearance of an extensive varicella exanthem became feverish, irritable and restless. On the following day, there occurred two generalised convulsions, the second lasting thrity minutes. The child died during the third convulsion, which occurred that night. Examination of the cerebrospinal fluid obtained post mortem revealed 20 mononuclear cells per cubic millimetre. Globulin was absent, and the fluid was sterile.

The lesions found in encephalitis following vaccination are characterised by perivascular degeneration of the myelin in the white matter, accompanied by a marked glial proliferation around these vessels. Active phagocytosis of lipoids is present in these zones of destruction of myelin. In these conditions the encephalitic changes are sharply limited to the white matter: there is neither destruction of myelin, perivascular glial proliferation nor degeneration of ganglion cells in the gray matter. However, in the case of encephalitis following chickenpox, herein reported, perivascular demyelinization and accumulations of fat-granule cells were present, but, in addition, there was a widespread involvement of ganglion-cells and a complete absence of glial proliferation. The changes of the ganglion-cells correspond rather closely to those described in acute, nonsuppurative encephalitis, but the formation of glial reticulum, hypertrophy of the endothelial and hyperplasia of the adventitial cells of bloodvessels described by Low in that condition were absent in the case

under discussion. Thus this case of encephalitis following chickenpox had certain features characteristic of both the encephalitis following vaccination and that following measles and the nonspecific encephalitis described by Low.

R. M. S.

[52] **Pneumocephalia intracranialis spontanea.**—L. Guttmann. *Zeits. f. d. g. Neurol. u. Psychiat.*, 1930, cxxviii, 82.

This is a useful summary and critical analysis of the condition in which air or gas of one or other kind appears within the cranial cavity, above or below the meninges, or in the cerebral substance, as a consequence of injury or for other pathological reasons. A schematic classification of the known varieties is offered, and a personal case described, with references to the cognate literature.

J. S. P.

[53] **Neurologic complications of pernicious anæmia.**—William Needles. *Arch. of Neurol. and Psychiat.*, 1931, xxvi, 346.

Of eleven cases of pernicious anæmia, complicated by subacute combined degeneration, in which adequate treatment with liver was given, signs of subacute combined degeneration developed in five despite therapy. Four cases remained stationary as a result of treatment, while in two cases some evidence of improvement occurred. These figures indicate that in appraising the value of the use of liver as a means of therapy neither complete pessimism nor complete optimism is justified. Why some patients do well while others fail to rally is a problem requiring further study. With regard to patients treated with liver before the onset of nervous complications, despite the favourable observations of Minot and Murphy the reports of other observers show that early and adequate liver treatment is by no means an absolute safeguard against the onset of neurological signs.

R. M. S.

PROGNOSIS AND TREATMENT.

[54] **The radical treatment of traumatic epilepsy and its rationale.**—Wilder Penfield. *Can. Med. Assoc. Jour.*, 1930, xxiii, 189.

A series of four cases are described in which operation for the relief of epilepsy following head injury was undertaken, with good results. Much stress is laid on the value of encephalography. It is pointed out clearly that epileptic attacks are most likely to occur, whatever the site of the wound, if the dura is penetrated and the cerebral substance injured, however moderately. From

a long series of experiments the author has been able to determine that wounds of the brain give rise to two differing types of sequel. A wound which leaves behind it destroyed cerebral tissue results in an extensive glial and connective-tissue scar, well vascularised, which exercises traction on the brain as it continues for a period of years, say, and causes the ventricles to be pulled towards it. This pull, and the plexus of vascular neoformation caught in it, are regarded as of importance in the etiology of focal epilepsy. On the other hand, if cerebral tissue is cleanly excised there results a fluid-filled space without a core of scarred connective-tissue, with little or no gliosis, and with no increase in vascularity. By comparison, such a region is of no pathogenic significance, or little, in respect of subsequent epileptic seizures.

The author considers therefore that clean, radical excision of contracting areas is justifiable, the necessary precautions being taken so as not to remove 'innocent vital areas.' J. V.

[55] **Chirurgico-therapeutic experiences with epileptic cases** (Pathophysiologische, pathohistologische und chirurgisch-therapeutische Erfahrungen bei Epileptikern).—L. GUTTMANN. *Zeits. f. d. g. Neurol. u. Psychiat.*, 1931, cxxxvi, 1.

THE author describes in much detail a series of some twelve cases of epilepsy, of varying duration but mostly more or less chronic, in some (though not apparently all) of which a history of one or other kind of head injury was forthcoming. He urges the usefulness of encephalography, claiming that in some instances it has furnished valuable information not revealed by ordinary clinical examinations. The serviceableness of operative interference must always be supplemented by medical means; it is wrong in theory and practice to cease the administration of sedative drugs merely because the patient has been successfully operated on. Just as an abdominal case requires dietary and other medical treatment after operation, so does a cerebral case of symptomatic epilepsy.

The paper also contains interesting data bearing on the localisation of function in the cortex. S. A. K. W.

[56] **Disseminated sclerosis treated with haemolytic serotherapy** (Nouveaux cas de sclérose en plaques traités per sérotherapie hémolytique).—M. LAIGNEL-LAVASTINE and N. T. KORESSIOS. *Bull. soc. méd. hôp. Paris*, 1930, No. 35, 1.

FOR several years now the authors have been treating cases of disseminated sclerosis by the method of hæmolytic serotherapy, the latter of the two having devoted his Paris *thèse* of 1930 to the subject. The principle of treatment is

based on the employment, for affections considered to be caused by an unknown virus, of a serum derived from the red blood corpuscles and spinal fluid of patients suffering from disease due to a neurotropic virus. In the present communication a series of fresh cases are described, from which the following conclusions are derived :—

1. In the interval between attacks the application of the method prevents the return of acute exacerbations (two cases thus treated : patients under observation for one year).

2. In the first months of the disease, whatever its form, mild or severe, serum effects a functional and organic cure (eleven cures in eleven cases of the kind : two cases followed for four years, one for three, and eight for one). Exception must be made of the rare cases in which the unknown virus rapidly produces definite sclerotic lesions (one case observed). Such cases are characterised clinically by complete absence of spontaneous remission. In the case mentioned the hæmolytic serum appears to have arrested extension of the process.

3. It is of value in cases older than one year and in others older still, with undeveloped symptomatology (one case followed for four years, four for three, 33 cases studied in France during the last two and a half years and eleven elsewhere, for more than one year). In these 49 cases the result of serum treatment has been amelioration more or less pronounced according to circumstances, very soon after the first injections in small doses. The improvement is both organic and functional : in many cases the Babinski sign has been modified immediately after injection. No severe relapse or exacerbation has occurred. Chronic cases and those of a serious character developing in the course of two or three years have been favourably influenced in about 50 per cent. (of 30 cases).

J. V.

[57] **Treatment of tabetic (genuine) optic atrophies with sulphur.**—J. FRIED. *Jour. Nerv. Ment. Dis.*, 1931, lxxiii, 487.

TWELVE cases are quoted. The author considers it important to emphasize the fact that cases with strong general reaction showed marked improvement of the eye functions. Cases however which reacted with slight general reaction were not much influenced by the sulphur treatment. Comparing the results obtained with other methods in treating optic atrophies, he states that among twelve cases treated with sulphur, six showed marked improvement, four presented improvement, one remained unchanged for a relatively long time of observation, and only one case became worse. Although remissions normally occur in optic atrophies this treatment seems to show sufficient promise to make further clinical trials desirable.

R. G. G.

[58] **Radical operations for major trigeminal neuralgia.**—C. H. FRAZIER. *Jour. Amer. Med. Assoc.*, 1931, xcvi, 913.

DR. FRAZIER has operated on 654 cases of facial neuralgia among 1,317 cases seen in 30 years, by the major method with which his name may be associated, and in the course of his experience mortality has been reduced to 0·26 per cent. Beginning with section of the sensory root in 1901, he started the procedure of subtotal resection—that is, with conservation of the ophthalmic portion of the root—in 1915. From 1918 he has also practised operation without touching the motor root. In his hands the operation as now conceived has proved entirely satisfactory. This paper recounts his experience and adds details to which attention may be directed.

S. A. K. W.

[59] **'Dial' as a surgical anæsthetic for neurological operations; with observations on the nature of its action.**—J. F. FULTON, E. G. T. LIDDELL, and D. M. RIOCH. *Jour. of Pharmacol. and Exp. Therapeutics*, 1930, xl, 423.

DIAL, the trade name for a liquid preparation of diallylbarbituric acid, is a satisfactory anæsthetic for major neurological operations on monkeys, cats and dogs. In monkeys there is a large margin of safety between the anæsthetic and the lethal dose. For the animals mentioned 0·4 to 0·5 c.c. per kilogram intraperitoneally is adequate.

Dial produces a state akin to normal sleep. Its site of action appears to be in the deep nuclei, chiefly in hypothalamus and medulla. In 100 operations under dial of the kind mentioned only one fatality was attributable to the anæsthetic.

J. S. P.

Endocrinology.

[60] **Innervation of the thyroid gland: (1) The presence of ganglia in the thyroid of the dog.**—J. F. NONIDEZ. *Arch. of Neurol. and Psychiat.*, 1931, xxv, 1175.

THE present article deals with the structure of ganglia found in the thyroid of the dog.

The author's descriptions clearly indicate that the thyroid of the dog, investigated from the standpoint of its innervation, may possess typical ganglia embedded in the parenchyma. The same is probably true of other mammals, including man.

That no ganglia have ever been described in sections of the thyroid of

the dog stained with routine methods is rather surprising since their neurons are quite large. But since the ganglia may be widely scattered, and are usually of small size, unless complete series of sections of whole thyroid lobes are examined it is easy to miss them. In new-born or very young puppies the task is considerably simplified, especially when neurofibrillar methods of staining are used. The latter stain the neurofibrils in the cell-bodies and dendrites of the neurons, thus removing any possible doubt as to the nervous nature of these elements. It must be stated, however, that successful impregnation of small ganglia in glandular organs is usually difficult, the chances of success depending largely on the technical skill of the investigator.

The idea that the ganglion-cells of the thyroid have entered the gland accidentally does not find support in the observed facts. The presence of fibres effecting connections with the neurons in the ganglia strongly indicates that the latter receive impulses from the central nervous system through preganglionic fibres. It is possible that some of the latter arise from the spinal cord and reach the thyroid after crossing the cervical sympathetic. However, the fact that the thyroid develops as a diverticulum of the floor of the embryonic pharynx suggests that the preganglionic fibres may come from the same source as many of the corresponding fibres supplying the ganglia of the alimentary tract (the descending colon excluded), viz. from the vagus. If such is the case, then the thyroid would also be supplied by the parasympathetic division of the autonomic nervous system.

The fact that some thyroids contain numerous neurons grouped into definite ganglia or appearing as elements scattered along the path of the nerves, and that in other glands neurons are very rare, suggests that their function is not primarily related to secretory phenomena in the follicular cells. In all probability they are concerned in the regulation of the circulation of the organ. In this regard it should be remembered that in many dogs there is no inferior thyroid artery. Even when present this vessel is much smaller than the superior thyroid artery. The presence of a double blood-supply in some thyroids may necessitate the existence of regulatory nervous mechanisms to facilitate the distribution of blood flowing in nearly opposite directions through vessels of unequal size, and arising from arteries of large calibre.

R. M. S.

[61] **The effect of thyroid administration on the blood cholesterol.**—A. Glen Duncan. *Jour. of Ment. Sci.*, 1931, lxxvii, 332.

Twenty-two cases were investigated, all of them male patients in a mental hospital. They included eight cases of dementia præcox, four of melancholia, one of mania, three imbeciles, one confusional case, one insanity with epilepsy, one paralysis agitans, one postencephalitic, and two general paralytics. In three of the eight dementia præcox cases a definite improvement coincided

with the diminution of serum cholesterol; two of these were extremely dull, brightened considerably under treatment, and became apathetic after its suspension; the third, a very deluded man, full of bitter complaints, lost his delusions and became mildly hypomaniacal, remarkably pleased with himself and all around him; he also returned to his former state when thyroid was stopped. One dementia præcox patient became worse and was more hostile. In one melancholia case increased agitation was the result. The one maniacal patient remained so until about three weeks after cessation of thyroid, when considerable improvement coincided with a great increase of blood cholesterol. The remaining patients showed no mental change, except that both general paralytics became less amenable and more difficult to nurse. The patient with a postencephalitic condition soon showed signs of thyroidism, and in the case of paralysis agitans the tremor was increased. Evidently any change accompanying thyroidic diminution of blood cholesterol will result from the increased excitability of the nervous system.

C. S. R.

[62] **Neuro-hypophyseal substance and erection** (Neuro-ipofisi ed erezione). —G. Roasenda. *Riv. di pat. nerv. e ment.*, 1931, xxxvii, 75.

In a patient affected by syphilitic myelitis with urinary incontinence and complete absence of sexual stimuli and erection for two years, the injection of certain preparations of neuro-hypophyseal substance provoked, together with other phenomena, a reestablishment of the functions of the bladder, and an immediate erection after a single injection. Thereafter a gradual and progressive return, after a certain number of these, to normality of the sexual function took place. The author compares this particular result with the already well-established influence of neuro-hypophyseal products on smooth muscle in general, and discusses with reference to this case the factors governing the phenomenon.

R. G. G.

Psychopathology.

PSYCHOLOGY.

[63] **The emotional value of dress.**—J. C. Flugel. *Psyche*, 1931, xii, 49.

The three functions of dress are related to decoration, modesty, and protection. The first two are purely psychological in nature and the third corresponds to certain needs of the mind as well as of the body. Modesty and decoration originate in opposed instincts and impel to contrary actions. Phylogenetically, decoration is the chief motive, and modesty comes later. Protection only

later plays any considerable rôle. In the case of the individual, the order is reversed. The child is at once protected, then ideas of modesty are taught, and the decorative point of view only awakens at adolescence. A child's satisfaction in nudity arises from auto-erotic and narcissistic elements and both these forms of pleasure are diminished by dress. The adult attitude to dress depends largely on the psychological reactions to the above-mentioned childish forms of gratification. Some achieve a real sublimation and displace the primitive interest in the naked body on to an interest in clothes themselves. Exhibitionism seeks to accentuate certain parts and this applies to the sublimation of exhibitionism by clothing. Many articles of dress have not only this value but also a symbolic significance.

The normal adult man has a more restricted narcissism and is less charged with erotism in dress. Modesty does not require him to cover his head, face, chest, or legs, and because of the greater rigour of his super-ego there is a severity of form and monotony of colour in his clothes. Concerning the auto-erotic elements—cutaneous and muscular—the woman enjoys a much greater liberty. She freed herself from the heavy and constricting clothes she used to wear in the nineteenth century at the same time as she became emancipated from many psychic and social restrictions. This has been accompanied too by a decrease in the severity of her super-ego. In man this tendency accounts for the modern dress reform movement. The erotic value of women's clothes depends a great deal on their capacity to suggest, reveal, or accentuate the shape of the body they cover. Homosexual women, with masculine identification, will wear clothes like the man's and find the same kind of satisfaction.

Certain more specific tendencies show themselves in the successive manifestations of fashion. (1) Decoration and modesty vary in their relative influence. Sometimes exhibitionism triumphs over modesty and at other times puritanism demands seriousness and simplicity. (2) There is a variation in the amount of displacement of the exhibitionistic interests from the naked body on to dress. (3) There are variations concerning the part of the body emphasized by the prevailing fashion. (4) There exists a variation concerning the age at which a woman is most admired.

Already we are beginning to see a reaction against these modern tendencies; a reaction in which we find a certain correlation between the variations that have been pointed out. Considerable forces, however, oppose this return to maturity. C. S. R.

[64] **The comparative psychology of Jews and non-Jews: A survey of the literature.**—J. RUMYANECK. *Brit. Jour. of Psychol.*, 1931, xxi, 404.

HERE an attempt is made to collate the judgements that have been passed on the psyche of the Jew and especially on his intelligence, which is supposed to be superior to that of other peoples. The results of a number of intelligence and

emotional tests that have been applied are critically examined, and the view is expressed that the claims of intelligence testers as being able to reveal innate psychological differences among different groups have in no way been substantiated : that although the Jews may be intellectually superior and may possess unique psychological faculties, no technique is in existence at present for their evaluation. The former trend in thought which ascribed to heredity or nature preponderant weight in the formation of these psychological differences is found to be untenable, and the view is suggested that in dealing with large groups of people as distinct from special family lines environment is of overwhelming and pervasive importance. C. S. R.

[65] **The psychology of the alcoholist.**—A. E. Carver. *Brit. Jour. Med. Psychol.*, 1931, xi, 117.

The alcoholist is a highly sensitive self-indulgent individual with an extremely easily wounded *amour propre*. Self-criticism no less than the adverse opinion of others is peculiarly irritating to him. He seeks to evade all responsibility for his maladjustment and blames any circumstance rather than himself. He suffers from a feeling of inferiority and desires excessively the society, sympathy and love of his fellows. Boastfulness and confabulation conspicuously cover his inferiority complex, whilst conviviality and intimate contact with his fellows afford occasion for the release of obscene wit and homosexual trends.

Alcohol, by producing euphoria, blunting the critical power and progressively relaxing inhibitions, permits of a flight from reality which up to a certain point is pleasurable, but when it is pushed too far regression proceeds to lower psychological developmental levels and the return of the repressed from these levels causes great anxiety and antisocial behaviour. Thus in the long run alcohol is liable to defeat the ends for which it is taken.

C. S. R.

NEUROSES AND PSYCHONEUROSES.

[66] **Stuttering.**—Smiley Blanton. *Mental Hygiene*, 1931, xv, 271.

Stuttering is regarded as a difficult combination of organic and constitutional and functional factors that requires speech training, such as may be used for the training of the speech and voice of non-stutterers, and also a definite knowledge of mental hygiene in order that hampering emotional fixations may be resolved. These emotional problems cannot be adequately treated by good will and a kind heart and inspirational talks. It is believed that an adequate treatment of stuttering must combine physical hygiene, mental hygiene, and speech training in a unified and well-rounded manner.

C. S. R.

[67] **The significance of a neurotic reaction as a precursor of schizophrenias.** —W. M. HARROWES. *Jour. of Ment. Sci.*, 1931, lxxvii, 375.

AFTER a brief history of dementia præcox and the neuroses, some clinical examples are given of cases illustrating the relation of neurotic symptoms to schizophrenia. In order to ascertain the incidence of the type of case under discussion, a series of 100 schizophrenic reaction types were investigated. Of the total cases, 29 patients made readjustments, which have been maintained in 22, who have therefore recovered; while seven have made a partial readjustment only, and are not functioning members of society, although they do not require to be in hospital. Out of this group of 29 it was found that nine cases showed sufficiently marked symptoms of a neurotic type in the prodrome to justify their inclusion in the variety of case under consideration. Out of the total 26 examples could be demonstrated as having a neurotic reaction first and later psychotic.

The points of importance are that a progression from a neurotic to a psychotic reaction not uncommonly takes place. The neurosis may be clear-cut, and may exist as a condition in its own right, without psychotic features, for a considerable period of time. The pre-occupations or content of thought can be shown to be the same during the neurotic and the psychotic phase. It is suggested, therefore, that the difference between neurosis and psychosis is in a large measure one of degree in the same process of mal-reaction to some psychic difficulty. The findings give grounds for a more cautious view of neurotic reactions, and a less pessimistic attitude towards the schizophrenic.

C. S. R.

PSYCHOSES.

[68] **A study of some schizoid children.**—A. T. CHILDERS. *Mental Hygiene*, 1931, xv, 106.

SOME observations are given here on 114 problem children of various types referred to a child-guidance clinic. Particular attention was directed to 19 of these cases which were called 'schizoid' children. Comparisons were made between the total group and the smaller special group, particularly in the matter of phantasy productions. While no syndrome was formulated to facilitate diagnosis and prognosis, several criteria were utilized in judging the nature and extent of the children's maladjustment. These were (1) the nature and extent of the child's social incapacity; (2) his habitual reaction to the situations and requirements of reality by withdrawal rather than by attack or by conforming; (3) the nature, extent, and purpose of his phantasies;

and (4) the occurrence in a given child of such definite mental symptoms as are usually observed in adult schizophrenics.

There was no evidence that these children were inherently different at birth from any other group of children. Nevertheless the social histories, as well as the statements of the children themselves, indicated strongly that such physical deviations as existed acted as handicaps or were used as such by the children in their adjustment. In every case a set of circumstances was found that might well explain the general or habitual attitude of withdrawal from the social requirements expected of the average child. In 13 out of the 19 cases, the child was found to be occupying an unusual position in the family. A large number, too, had passed a comparatively long period in circumstances that to a considerable degree prohibited normal play or other associations with other children. While the 19 cases termed schizoid fell into the age-group from 10 to 16 years, this is not to be taken to mean that these children had not in earlier years shown developments in the direction of retreat from social adjustment. On the other hand, it would seem that the greatly increased social demands of this period intensified their struggles and served to bring out a more clear-cut picture of the syndrome.

These children are all difficult to treat and the older they are, the less satisfactory treatment is. The causative factors, chiefly to be found in the family life and all of them deep-seated, are not easily modifiable. It is believed that in cases of this type there is serious mental illness in the making. Many such children, unless their lives are radically changed, will in due time become the psychotics of adulthood. The psychosis will very likely be a schizophrenia.

C. S. R.

[69] **A statistical study of delusions in the manic-depressive psychoses.**—KARL M. BOWMAN and ALICE F. RAYMOND. *Amer. Jour. of Psychiat.*, 1931, x, 111.

THIS study was made in 1009 cases of manic-depressive psychosis, with 1408 cases of schizophrenia and 496 cases of general paresis as controls. Delusions were absent in 43 per cent. of the males and 41 per cent. of the females in the manic-depressives as compared with 10 per cent. of the males and 7 per cent. of the females in schizophrenia, and 39 per cent. of the males and 42 per cent. of the females in general paresis. The most common type of delusion in the manic-depressives was the persecutory type, which was present in 20 per cent. of the cases. This delusion was also the most common in schizophrenia, 54 per cent. of the males and 58 per cent. of the females having this type. In paresis the persecutory delusions were much the same as in the manic-depress-

ives, but males showed 27 per cent. and females 12 per cent. of grandiose delusions, indicating that these latter are the most common type to occur in general paralysis. The schizophrenic group show a consistently higher percentage of religious and erotic delusions than do the manic-depressives, whereas the grandiose and hypochondriacal delusions show no significant differences. Marital condition had apparently little to do with the type of delusion and age showed nothing of significance except that in persons with schizophrenia delusions were less frequent among the younger. The pre-psychotic personality and intelligence of the patient seemed to show several significant associations with the number and types of delusions. Considerable correlation existed between delusions and hallucinations, the most striking being between persecutory delusions and auditory hallucinations, which show a positive association in all groups except schizophrenic females. The occurrence of a previous attack seemed to have no important effect upon the number of types of delusions for all three types of mental disorder. With regard to alcoholic habits the only important findings seem to be that no delusions occur more frequently in schizophrenic and general paretic males who are abstinent, than in schizophrenic males who are temperate. There was no significant association between the white blood count and delusions.

C. S. R.

PSYCHOPATHOLOGY.

[70] **Experimental catatonia in animals and man** (Catatonia sperimentale negli animali e nell'uomo).—V. M. Buscaino. *Riv. di pat. nerv. e ment.*, 1930, xxxvi, 593.

Certain substances, notably bulbocapnin and somnifen, when injected into animals or man produce symptoms identical with those observed in catatonic dementia præcox and postencephalitic parkinsonism. These substances have the structure of amines and provoke the symptoms by an extracortical action, with a preference for the basal ganglia. This suggests that in the above-mentioned diseases the symptoms may be due to a poisoning by the amine group.

R. G. G.

[71] **Researches on the action of bulbocapnin in man** (Ricerche sull'azione della bulbocapnina nell'uomo).—U. de Giacomo. *Riv. di pat. nerve. e ment.*, 1930, xxxvi, 423.

Bulbocapnin is an alkaloid extracted from *corydalis cava*. The author conducted experiments of administration by the mouth and intramuscularly, and

then tried its use intravenously, and found that by this method he could provoke a transitory aggravation of the cataleptic symptoms in cases of dementia præcox. He also succeeded in producing a fleeting catalepsy in some subjects (psychasthenic and epileptic) who before the experiment had not shown any traces of such phenomena. In two subjects also there were observed short crises of excitement and loss of consciousness. In view of a comparative analysis of the various phenomena, the author draws a parallel between the syndrome induced by bulbocaphin in man and that of catatonia. The resemblance to the latter is closer than in the case of parkinsonism.

R. G. G.

[72] **Experimental hormonal catatonia** (Hormonale experimentelle Katatonie).—H. DE JONG. *Proc. Kon. Akad. v. Wetensch. te Amsterdam.* 1931, xxxiv, No. 4.

CONTINUING his line of experimental approach to the question of dementia præcox (see this JOURNAL, vol. xi, p. 275), Dr. de Jong has found that adrenalin and acetylcholin, in certain doses, are capable of producing in higher animals a symptom-complex comparable with the motor phenomena of catatonia as seen in psychotic cases. It must be expressly noted, however, that these hormones are not the only substances capable of causing experimental catatonia, but those they are, in point of fact, the sole substances found in human metabolism which as yet have been demonstrated to exercise such an effect. The experiments lend some support to the view that a disorder of internal secretion is causally connected with the development of dementia præcox.

S. A. K. W.

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[73] **Insulin poisoning with acute mental confusion and aphasia as cause of a traffic accident** (Insulinvergiftung mit akuter Geistesverwirrheit und Aphasie als Ursache eines Verkehrsunfalles).—J. FOG and M. SCHMIDT. *Deut. Zeits. f. d. g. ger. Med.*, 1931, xvi, 376.

THE patient was a young chauffeur of 25 who ran his car with force into another motor vehicle in circumstances where no accident whatever should have occurred. When questioned, his answers were so confused as to suggest alcoholic excess, but of this there was no evidence. Paraphasia and jargonaphasia were pronounced, and the mental confusion and disorientation complete.

It eventually transpired that he had been suffering from diabetes for some six years, and been treated with insulin for five. On the morning of the acci-

dent, two and a half hours before it, he had had an injection of 10 insulin units, without breakfast, though he took something to eat at the time. Two hours later he suddenly felt hungry and began to eat while driving. Apart from the hunger he had none of the usual insulin symptoms, and could remember, in part, the incidents thereafter. Blood sugar estimated two hours after the accident was ·075 per cent.

Both the aphasia and some of the other psychical symptoms exhibited an intermittent character, and eventually passed off. The authors ascribe the phenomena to hyperinsulinism, and refer to analogous cases from the literature.

S. A. K. W.

[74] **Anatomical lesions and mental disturbances in disseminated sclerosis** (Le rapport des lésions anatomiques à l'évolution des troubles mentaux de la sclérose en plaques).—J. HANDELSMAN. *Roczn ika Psychjat.*, 1931, xiv, 1.

IN five cases out of 29 the author has found marked psychical disorders, as follows: symptoms recalling manic-depressive psychosis; depressive psychosis; mania of persecution, stupor, and auditory hallucinations; cyclothymia accompanied by mania of jealousy and depression: and a syndrome like that of general paralysis. These diverse phenomena occurred in episodic fashion, mainly at an early stage, and some recurred at intervals over a period of years.

Evidence is adduced which goes to show that such mental symptoms, together with those of a milder character but of the same series, vary with neurological symptoms. At later stages a state of psychical passiveness, with puerility and weakening of vital energy in respect of intellectual functions, may be observed.

After a full description of the two main types of histological lesion, acute and chronic, characterising the disease, the author remarks that in his opinion the mental symptoms do not depend on the quantity of such lesions, but on their quality. Mental disorders are apt to develop when, anatomically, recent and acute lesions are to be found. They belong to the type of 'exogenous psychosis' of Bonhœffer: others, however, more or less resemble the organic psychotic syndrome of Bleuler.

S. A. K. W.

[75] **The cytology of the spinal fluid in general paralysis and its variations after malaria-therapy studied with vital colorisation** (La citologia del liquido cefalo-rachidiano nella paralisi progressiva e le sue variazioni dopo la malarioterapia studiate con la colorazione vitale).—C. UGURGIERI. *Riv. di pat. nerv. e ment.*, 1931, xxxvii, 54.

THE author has examined sixty different fluids with vital colorization. In 48 fluids of paretic patients it is confirmed that in this clinical form of nervous

syphilis, the cells are notably polymorphic and that plasma-cells are always present in a greater or less quantity. In 17 cases examined before and after malarial therapy, it was shown that there was no parallel between the cytological and serological formula of the fluid and the mental condition of the patient. It confirms the importance of the examination of the cytological formula, which can be easily carried out by the method of vital colorization, as an indication of the diminution or disappearance of acute conditions in the meninges and parenchyma in paresis after malarial therapy.

R. G. G.

PROGNOSIS AND TREATMENT.

[76] **Some effects of the inhalation of carbon dioxide and oxygen, and of intravenous sodium amytal, on certain neuropsychiatric conditions.**—H. C. Solomon, M. R. Kaufman, and F. D. Elseaux. *Amer. Jour. of Psychiat.*, 1931, x, 761.

By means of moving pictures the effects of the inhalation of high concentrations of carbon dioxide and of sodium amytal given intravenously was noted in neuropsychiatric patients. The experiments follow the work of Lorenz who considered that part of the psychotic manifestation of catatonic-like stupor was due to inefficient respiratory activity. In the first case, that of a woman whose diagnosis rested between that of a benign stupor and a catatonic-schizophrenic condition, it was found that after breathing a mixture of 40 per cent. carbon dioxide and 60 per cent. oxygen for two or three minutes, the patient became quite normal in her responses and activity. The period of lucidity lasted for 15 to 25 minutes. Then a confused expression was shown, movements slowed, there was difficulty in memory responses, and soon the original state was regained. It is interesting to note that in the course of a few months this patient began to show a definite improvement. The second case was a catatonic dementia præcox. After the inhalation of the gas mixture the patient was much brighter, talked, dressed himself quickly, made himself neat, and showed lively rational movements. The third one was in the terminal stage of a catatonic dementia præcox. The gas produced violent convulsive movements following which the patient sat up and talked a 'word-salad' replete with obscenity. Two other patients who were suffering from very marked Parkinsonism after epidemic encephalitis and who were unable to get off the bed or walk showed definite change. In both the tremor was first increased but later this was less, and also the rigidity. One could move somewhat and the other was able to get up off the bed and walk about the room. In a patient with a negativistic, mutistic syndrome, an injection of sodium amytal produced marked results. He showed normal expression, talked fairly freely, and was reasonably co-operative. In half an hour he relapsed into his former state.

It has been the authors' experience that patients with long-standing schizophrenic symptomatology show less response than do the patients in more acute attacks or those whose cases seem to fall more properly into the group of benign or toxic infective stupors. With those whose cases are of long-standing, the most that happens is a 'word-salad' response, suggesting this may be the full capacity of the cerebral process at the time.

It is assumed in the case of the stuporous patients that there is a reduced activity of cerebral neurones, perhaps dependent upon an interference with the normal metabolic activity of the cell. With the inhalation of the gas there is possibly a further lessening of metabolic activity resulting in lessened activity of the neurones and in the clinical manifestation of a loss of consciousness. With the cessation of carbon dioxide these processes are relieved from interference, with the result that they seek the point of equilibrium maintained previous to the inhalation. In so doing they are necessarily speeded up and may overstep the previous point of equilibrium—that is, may approximate to a more normal degree of metabolic activity with a consequent more normal degree of nervous activity shown by more normal contact with their environment. This hypothesis would similarly explain the situation in regard to sodium amytal anæsthesia.

C. S. R.

[77] **Malaria-therapy in schizophrenic conditions** (La malarioterapia nelle forme schizofreniche).—G. B. Belloni. *Riv. di pat. nerv. e ment.*, 1931, xxxvii, 508.

After giving a critical digest of the literature on the subject the author refers to a series of 19 cases of dementia præcox treated by malaria therapy. These included hebephrenic and catatonic forms, and also patients in the last stages of the disease with extreme mental enfeeblement. The author is favourably impressed with the application of malaria therapy in dementia præcox, having seen some cases of cure, as he alleges, and none of serious danger.

R. G. G.

[78] **Group treatment of the psychoses by the psychological equivalent of the revival.**—L. Cody Marsh. *Mental Hygiene*, 1931, xv, 328.

The writer comes to the following conclusions. More patients receive psychiatric attention than is possible by the individual method. Thus many are helped who might not be helped otherwise. They receive the beginnings of a mental and emotional reeducation and obtain varying degrees of emotional release. Many are motivated toward improvement and recovery and they work out their social difficulties in the class toward a successful issue. The

emotional and mental streams are extraverted at the social level. Patients are made more accessible for the individual approach, are made in every way better hospital citizens and their morale is improved. The class hour for most of them is an hour of happiness. It is too early to draw any conclusions as to relation of diagnosis to the success of the group treatment. While the functional cases are necessarily the most hopeful, many organic ones have been thus helped. The method fills the great need of providing a presentation of reality which is more attractive and more potently motivating that the ideas and situations that motivate mental disease. In order that the most can be made of the group approach, it is recommended that communities of mental patients be thought of as schools rather than as hospitals, that the psychiatrist be preeminently an educator, and that the victim of a psychosis be regarded rather as a student to be reeducated than as a patient. While the writer believes that the group approach is a necessary part of the treatment of mental disease, he urges it as an addition to what we already possess, and not as substitute. Individual treatment will still be required in every case.

C. S. R.

Reviews and Notices of Books.

Medical Psychology : The Mental Factor in Disease. By WILLIAM A. White. Nervous & Mental Disease Monograph Series, No. 54. New York and Washington : Nervous & Mental Disease Publishing Co. 1931. Pp. 141.

THIS well known writer endeavours to show that disease in any part of the body, however it may be caused, has in every instance a psychological aspect. The various chapters logically lead up to this conclusion. The fundamental biological concepts necessary for the understanding of such psychological questions are presented at some length. The organism-as-a-whole is first studied from the point of view of its developmental integration and structuralization and then the factors which render it dynamic are pointed out. The thesis is that the unique character of a mental reaction is that it is a total reaction, that the field of psychology is the field of total reactions, and that the field of partial reactions belongs to the domain of physiology. A discussion, mainly biological, undertakes to establish the conception of mind as introjected environment. After dealing with the structure and functions of the psyche—very largely based upon Freudian lines—chapters are devoted to the mental mechanisms found in psychopathology and the psychological factor in disease.

These few pages are pregnant with suggestive and stimulating material and written in Dr. White's usual lucid and attractive style. No better insight into the basic concepts of medical psychology can be gained than by a careful study of this small work and the author's previous contribution, *The Foundations of Psychiatry*.

The Mental Defective : A Problem in Social Inefficiency. By RICHARD J. A. BERRY and R. G. GORDON. London : Kegan Paul, Trench, Trubner & Co. 1931. Pp. 196. Price 8s. 6d. net.

THE growing importance of mental deficiency in various departments of social life and the lack of knowledge on the part of manywho have to deal with the problems arising from it, have led the authors to present here the latest achievements in its study and in the underlying underdevelopment of the growing brain. The book, though intended to be popular and addressed partly to the general reader,

will be found to be of great utility to the average medical man who desires to orientate himself on the subject. Mental deficiency problems in their various aspects are simply dealt with and followed by chapters on the evolution of the brain and the making of mind. The different types of defectives are discussed, the relationship of mental deficiency to other forms of illness briefly spoken of, and its social consequences pointed out. A policy for the handling of the problem concludes the volume.

Feeble-mindedness is regarded as largely a recessive Mendelian unit-character. The defect cannot be cured but the condition should be recognized early and no time wasted in trying to fit the defective for that for which he is definitely unfit; he should be placed in an environment where he may lead a useful life within his limitations. It seems futile for the country to spend £93 per annum on the inefficient child and only £12 on the efficient one. Amongst suggested eugenic measures are: control of immigration; more discriminating marriage laws; a quickened national eugenic conscience; sexual segregation; and finally, drastic measures of asexualisation or sterilisation when necessary. The whole subject is dealt with comprehensively and clearly and in such a form that the aim of the book is very adequately fulfilled. Excellent illustrations add to its value.

Recent Advances in the Study of the Psychoneuroses. By MILLAIS CULPIN, M.D., F.R.C.S. London: J. and A. Churchill. 1931. Pp. 348. Price 12s. 6d.

WE can well believe Dr. Millais Culpin when he remarks in his preface that the writing of his book has presented peculiar difficulties. When a subject deals with common ailments whose manifestations are as definite as their etiology and, indeed, nomenclature are indefinite, he who would schematise their description must find himself rather seriously handicapped if he seeks to follow the canons of medical science. Thus the author sees it is essential to write a chapter, and that not one of the shorter, on 'nomenclature, classification, and diagnosis.' Its value in clearing the air is considerable, even if not all clinicians will agree with its conclusions. Of the etiology of the psychoneuroses, it is true, Dr. Culpin appears to be in little doubt; psychoneurosis is 'practically synonymous with a minor psychosis,' and 'neurosis' is a 'physiological disturbance' that can occur in any minor psychosis. The former can only be understood etiologically by holding some view, some theory, of mental processes apart from awareness, and the author announces that the chief advances in this respect have been the direct or indirect result of psychoanalytical discoveries. He devotes much attention to aspects of neurosis (or of psychoneurosis) with which he has made himself particularly familiar, viz. occupational

and industrial types, and this part of the book is informative and illuminating, since it is based on many original observations. Occupational 'cramp' is regarded as a symptom of a psychoneurotic kind comparable to stammers, tremors, and 'functional paralyses.' External physical causes are discarded by Dr. Culpin for psychoneurotic symptoms; miners' nystagmus is a symptom of a psychoneurosis differing in no way from others, and only the recognition of psychopathological principles in handling it will 'bring order into the mass of absurdities and contradictions that make up current views upon the subject.'

The last four chapters of the book are from other pens, and deal respectively with individual and analytical psychology, with the psychopathology of childhood and psychotherapeutic clinics.

Psychopathology and Politics. By Harold D. Lasswell, Assistant Professor of Political Science, University of Chicago. Chicago: University of Chicago Press. London: Cambridge University Press. 1931. Pp. 285. Price 13s. 6d. net.

Applied psychopathology was bound sooner or later to take within its sphere of activity politics and the politician. Behind various political moves in one country or another at all times, and more especially in the last two decennia in Europe (and elsewhere, for that matter), thinking minds must have concerned themselves with the personalities of the 'prime movers,' and have asked what manner of men they were and to what extent their political conduct was coloured, influenced, even originated, by motives and factors connected with their individual neural and psychological constitution and experience. Clearly, a study of this kind, if it is to be conducted on scientific lines in the light of contemporary knowledge of personality, demands opportunities that can not always be forthcoming; what is requisite is the lengthy scrutiny of the life-histories of specific individuals. Prof. Lasswell has made a commencement in this deeply interesting book, whose conclusions, in the author's words, are 'highly provisional though potentially significant.' Of the fundamental truth of not a few of his statements many must surely be already convinced: political discussion, instead of solving social difficulties, often complicates them, seeing that 'the discussion by far-flung interests arouses a psychology of conflict which produces obstractive, fictitious, and irrelevant values.' The problem of politics is 'preventive'; it is less to solve conflicts than to prevent them. For many politicians their political policy is symbolic of their own wants, and 'the individual is a poor judge of his own interest.' His adjustment is especially likely to be 'symptomatic rather than healthy

and reflective.' Political solutions are too often not those that are rationally best but merely such as are emotionally satisfactory.

However tentative the conclusions, as already remarked, the line of approach is bound to become more fruitful if only it can be pursued adequately.

Selected Writings of John Hughlings Jackson. Volume I. on Epilepsy and Epileptiform Convulsions. Edited by JAMES TAYLOR, M.D., F.R.C.P. London: Hodder & Stoughton. 1931. Pp. 500. Price 25s. net.

ALL students of neurology will welcome the appearance, in convenient form, of a series of papers written by Hughlings Jackson between 1861 and 1902, which deal with the subject that was peculiarly his own. Many of these were published in journals long since defunct, and have never perhaps received the serious attention they merit, for this and for other reasons. Probably only a few neurologists to-day have really been familiar with them, and we need not now ask what was their reception with, and influence on, those of a past generation. It suffices that the labour of love of their Editor should be fully appreciated to-day by all who hold Jackson's name in respect and affection, and by those of a new generation who can now go to the fountain head for scientific study of a 'disease' that is just as common as ever it was. New methods of inquiry and of research, of which Jackson was ignorant, cannot possibly discount the immense value of his own work, for the clinical phenomena remain the same.

The book is printed in a clear type, and possesses a long and carefully compiled index. The Editor's preface and introduction are explanatory of the purpose of the volume, which is indispensable to the student of the subject and which is assured of a cordial welcome by an ever widening circle.

The Treatment of Behaviour Disorders following Encephalitis. By EARL D. BOND, M.D., and KENNETH E. APPEL, M.D. London: George Allen and Unwin. 1931. Pp. 163. Price 8s.

THE scourge which epidemic encephalitis has become, more particularly as regards its aftermath of mental crippling in perhaps one-third, or more, of all cases that survive the original attack, has long been realised not merely by neurologists but by those who have to deal with the delinquent and the

'difficult child.' For it is clear from clinical and other records that, more especially in the case of the child, juvenile, and young adult, one of the consequences of epidemic encephalitis is an alteration in personality, so called, changing the individual concerned into a mischievous, unreliable, impulsive, and volatile being, whose conduct sooner or later brings him into conflict with domestic or public authorities.

This aspect of the question was the reason for the institution in England a number of years ago now of a special hospital unit to deal with cases of the kind, which has proved to be useful from both a social and a therapeutic point of view. The present monograph offers the reader a critical survey of experiences in America, in connexion with the University of Pennsylvania and Pennsylvania Hospital, of an analogous kind. Since December 1924, 48 post-encephalitic children (twelve years old and under) have been segregated in special quarters in the hospital because of 'bad behaviour,' together with a smaller number of apparently identical cases in which, however, no history of previous encephalitis could be obtained.

The authors affirm with conviction that bringing the children under psyciatric guidance, in groups, not merely lessens the damage they were inflicting on society, but also alters for the better the downward direction of their lives. For all the details of the methods employed this useful publication should be consulted; no little part of its value consists in the candour with which after-results are scrutinised, failures being investigated just as much as successes. Perhaps the feature that emerges prominently is the fact that the problems which postencephalitic children present are far from being solved.

Uber Apraxie. By Otto Sittig, Prag. Berlin: S. Karger. 1931. Pp. 248. Price not stated.

The study of apraxia has not perhaps attracted in recent years just as much attention as formerly: at least, it seems rather to have come under a cloud in view of current theories depreciating and deprecating efforts to correlate structure and function in the brain. Nevertheless no one who has had occasion to study clinically the phenomena of apraxia is likely to underestimate their localising value if he has the chance of comparing them with post-mortem findings. It is of much interest to find Dr. Otto Sittig contending firmly for the clinical significance and pathological importance of apraxic phenomena, but it is still more gratifying to note his steady adherence to a physiological as opposed to a psychological study of the subject. He animadverts on the confusion that has arisen by admixture of physiological and psychological terms—a comment applicable also, in full force, to the cognate subject of

aphasia—and seeks throughout to conceive of the derangement on physiological lines.

Appreciation of the historical part played by the researches of Hughlings Jackson in this respect, first pointed out by Wilson in 1908, and tardily acknowledged by Liepmann in 1920, is given by the author, who indeed ranges himself under a Jacksonian standard in endeavouring to apply to the study of apraxia the general Jacksonian rule that movements which are most automatic and least individual are least likely to be affected by cortical disease. Dr. Sittig devotes much attention to apraxia of trunk musculatures, having in the course of the last two years had occasion to observe no less than 17 cases in which it was possible to detect some disorder of this kind. The important relationship of apraxic symptoms to lesions of the corpus callosum and in the distribution of the anterior cerebral artery is well exemplified by a personal case, here reported at considerable length. It is pleasing to find that the author eschews the schematic divisions of the Wernicke school and adopts a more empirical approach to the problem.

The monograph is well illustrated and contains an excellent bibliography.

The Commoner Nervous Diseases. By FREDERICK J. NATTRASS, M.D., F.R.C.P., Assistant Physician, Royal Victoria Infirmary, Newcastle-upon-Tyne. London: Humphrey Milford, Oxford University Press. 1931. Pp. 218. Price 12s. 6d.

DR. NATTRASS has written, for general practitioners and students, a compendious yet concise volume dealing with the commoner nervous affections of the day, as seen in private and out-patient practice. An introductory chapter on principles of diagnosis, illustrated by a number of photographs and diagrams, precedes a careful, accurate, and readable account of such everyday nervous maladies as disseminated sclerosis, neurosyphilis, neuritis, cerebral tumour, meningitis, encephalitis, migraine, chorea, and so forth. Considerable attention is paid to epilepsy and cerebral vascular lesions, while symptoms such as vertigo also receive annotation. The book is thoroughly modern in its conceptions and practical in its discussion of questions of treatment. Interspersed through the text are brief illustrative accounts of personally observed cases. The author is familiar with current neurological literature, as appears from the various references in foot-notes to papers and books which supply further information on the particular point under examination.

The volume, we believe, will serve a useful purpose. No serious omission has been made, even if the author's decision as to what is common in neurology and what is not may not perhaps coincide with what others might

think. Nor does perusal reveal any particular mistake in fact or misjudgement of theory. To write a book of this kind, indeed, requires qualities of an exceptional nature, for the temptation to go beyond its intended scope must be considerable. We compliment Dr. Nattrass on a meritorious achievement.

Die Primare Verrücktheit. By KURT KOLLE, Privatdozent at the University of Kiel. Leipzig: Georg Thieme. 1931. Pp. 268. Price M.25.

THIS monograph deals in great detail with the subject of paranoia and paraphrenia on a largely empirical and clinical basis. Some 66 cases are investigated and subjected to minute analysis from psychopathological and genealogical aspects alike. The information supplied by the latter study is embodied in a series of tables of no little interest. Much attention is paid to the physical make-up and character of the patients, to semeiological forms and to the relation of paranoia to other psychotic types, by way of both comparison and contrast. Atypical varieties also receive consideration. Useful generalisations are reached in respect of prognosis, and there is some discussion of the forensic and hereditary problems furnished by the material examined. Between paranoia and paraphrenia, the latter being considered a definite though distinctly rare entity, differences of a more or less fundamental character are stressed. As a contribution to a somewhat vexed question it is more documentary and statistical than pathogenically illustrative, and contains no novel theory or descriptions; nevertheless the data here subjected to analysis have a good deal of value.

Transactions of the Sexual Reform Congress, London, 1929. Edited by NORMAN HAIRE, Ch.M., M.B., London. London: Kegan Paul. 1931. Pp. 670. Price 25s. net.

THE proceedings of the Sexual Reform Congress held in London under the auspices of the World League for Sexual Reform embody a long series of papers many of which have neither neurological nor psychopathological interest, and among which contributions of very unequal value are included, as may be supposed. Here and there, however, are to be found articles couched in a scientific setting and not cheapened by catch-penny titles or vitiated by patent prejudice. But the problem of sex has so many facets, and touches human activities at so many points, that it is well for different minds, with varying temperaments and outlooks, to deal with its many aspects seriatim, and a congress of this kind provides the opportunity.

I. Internationale Tagung für angewandte Psychopathologie und Psychologie, Vienna, 1930. Edited by H. HARTMANN, M. PAPPENHEIM and E. STRANSKY. Berlin: S. Karger. 1931. Pp. 241. Price M.17.50.

THE transactions of the first International Congress for applied psychopathology and psychology contain a number of communications which must prove interesting, and some valuable, to those whose line of work lies in these directions. It is impracticable to specify all which commend themselves, though that on 'Massenpsychose und Individuum,' by Prof. Erismann, by Dr. Hitschmann on 'Pathographia and Psychoanalysis,' and on 'Angewandte Psychopathologie und Gegenwartzivilisation' by Prof. Stransky may here be mentioned.

The Treatment of Schizophrenia. By L. E. HINSIE, M.D. London: Baillière, Tindall and Cox. 1931. Price 13s. 6d.

THIS book, except perhaps for beginners in the subject, does not fulfill expectations. Its psychotherapeutic pronouncements are elementary. Only one case is recorded in detail, and its later progress, which is the more interesting, is described only in general terms. The patient in question was most unusually accessible and self-critical, even for an early case.

The last chapter contains an uncritical summary of various modes of treatment apart from psychotherapy.

Nevertheless, the book fills a definite purpose in encouraging others towards an interest in the extremely difficult problem of the psychotherapy of schizophrenia.

The Recovery of Myself. By MARIA KING. With a preface by ADOLF MEYER. London: Humphrey Milford, Oxford University Press. 1931. Pp. 148. Price 9s.

IT is always instructive to hear a patient's point of view. We have here a simple and frank account of the experiences of the authoress who was a drug-taker and an inmate of a mental hospital for some months. The history of her varying mental reactions and how she gradually gained insight into the source and meaning of her maladaptations until she made a good recovery, makes interesting reading. Such a record materially helps to remove the ignorant prejudices popularly existing with regard to mental institutions. In her epilogue Miss King renders a warm tribute to the new revelations of psychology and their practical applications to psychiatry. She points out that it is not the mental sickness that we should be ashamed of but the inertia and prejudice which keep us from seeking such remedies.

The Unknown Self. By GEORG GRODDECK, M.D. The C. W. Daniel Company. 1931. Pp. 207. Price 7s. 6d.

THE basis of this book is that organic disease can not only be influenced but produced by psychological causes, and so can be influenced also by psychotherapy. There is introduced also the philosophising notion of an 'Es,' closely allied to the Freudian 'Id,' which is held responsible for the production and aggravation of the instances of organic disease mentioned.

Dr. Groddeck is a kindly physician whose ministrations are not only of curative but of euthanasic value, but his book can only be regarded as a popular exposition and not as a serious contribution to science.